McDonald JC; McDonald AD; Armstrong B; Sebastien P. Cohort Study of Mortality of Vermiculite Miners Exposed to Tremolite. *British Journal of Industrial Medicine*. 43:436–444. 1986.

McDonald JC; Liddell FDK; Dufresne A; McDonald AD. The 1891–1920 Birth Cohort of Quebec Chrysotile Miners and Millers: Mortality 1976–1988. *British Journal of Industrial Medicine*. 50:1073–1081. 1993.

McGavran PD; Butterick CJ; Brody AR. Tritiated Thymidine Incorporation and the Development of an Interstitial Lesion in the Bronchiolar-Alveolar Regions of the Lungs of Normal and Complement Deficient Mice After Inhalation of Chrysotile Asbestos. *Journal of Environmental Pathology, Toxicology, and Oncology*. 9(5-6):377–391. December. 1989.

McGavran PD; Moore LB; Brody AR. Inhalation of Chrysotile Asbestos Induces Rapid Cellular Proliferation in Small Pulmonary Vessels of Mice and Rats. *American Journal of Pathology*. 136(3):695–705. 1990.

Mercer RR and Crapo JD. Three-Dimensional Analysis of Lung Structure and its Application to Pulmonary Dosimetry Models. In *Toxicology of the Lung*, 2nd edition, Gardner DE; Crapo JD; McClellan RO (eds.). Raven Press, New York. 1993.

Middleton AP; Beckett ST; Davis JMG. Further Observations on the Short-Term Retention and Clearance of Asbestos by Rats, Using UICC Reference Samples. *Annals of Occupational Hygiene*. 22:141–152. 1979.

Miller FJ; Overton JH; Kimbell JS; Russell ML. Regional Respiratory Tract Absorption of Inhaled Reactive Gases. In *Toxicology of the Lung*, 2nd edition, Gardner DE; Crapo JD; McClellan RO (eds.). Raven Press, New York. 1993.

Moolgavkar SH; Dewanji A; Venzon DJ. A Stochastic Two-Stage Model for Cancer Risk Assessment. 1: The Hazard Function and the Probability of Tumor. *Risk Analysis*. 8(3):383–392. 1988.

Moolgavkar SH; Luebeck EG; De Gunst M; Port RE; Schwarz M. Quantitative Analysis of Enzyme-Altered Foci in Rat Hepatocarcinogenesis Experiments. Single Agent Regimen. *Carcinogenesis*. 11(8):1271–1278. 1990.

Moolgavkar SH; Luebeck EG; Krewski D; Zielinski JM. Radon, Cigarette Smoke, and Lung Cancer: A Re-Analysis of the Colorado Plateau Uranium Miners' Data. *Epidemiology*. 4:204-217. 1993.

Morgan A; Holmes A. Concentrations and Dimensions of Coated and Uncoated Asbestos Fibres in the Human Lung. *British Journal of Industrial Medicine*. 37:25–32. 1980.

Morgan A; Talbot RJ; Holmes A. Significance of Fibre Length in the Clearance of Asbestos Fibres from the Lung. *British Journal of Industrial Medicine*. 35:146–153. 1978.

Morgan A; Black A; Evans N; Holmes A; Pritchard JN. Deposition of Sized Glass Fibres in the Respiratory Tract of the Rat. *Annals of Occupational Hygiene*. 23:353–366. 1980.

Morrow PE. Issues: Possible Mechanisms to Explain Dust Overloading of the Lungs. *Fundamental and Applies Toxicology*. 10:369–384. 1988.

Mossman BT. Mechanisms of Asbestos Carcinogenesis and Toxicity: The Amphibole Hypothesis Revisited. *British Journal of Industrial Medicine*. 50:673–676. 1993.

Mossman BT; Churg A. Mechanisms in the Pathogenesis of Asbestosis and Silicosis. *American Journal of Critical Care Medicine*. 157:1666–1680. 1998.

Mossman BT; Marsh JP. Role of Active Oxygen Species in Asbestos-Induced Cytotoxicity, Cell Proliferation, and Carcinogenesis. In *Cellular and Molecular Aspects of Fiber Carcinogenesis,* Cold Spring Harbor Laboratory Press. 0-87969-361-4/91. pp. 159–168. 1991.

Mossman BT; Bignon J; Corn M; Seaton A; Gee JBL. Asbestos: Scientific Developments and Implications for Public Policy. *Science*. 247:294–301. 1990.

Mossman BT; Kamp DW; Sigmund A; Weitzman SA. Mechanisms of Carcinogenesis and Clinical Features of Asbestos-Associated Cancers. *Cancer Investigation*. 14(5):466–480. 1996.

Mossman BT; Faux S; Janssen Y; Jimenex LA; Timblin C; Zanella C; Goldberg J; Walsh E; Barchowsky A; Driscoll K. Cell Signaling Pathways Elicited by Asbestos. *Environmental Health Perspectives*. 105(Suppl 5):1121–1125. September. 1997.

Muhle H; Bellman B; Takenata S; Ziem Y. Inhalation and Injection in Rats to Test the Carcinogenicity of MMMF. *Annals Occupational Hygiene*. 31(4B):755–764. 1987.

Nario RC; Hubbard AK. Localization of Intercellular Adhesion Molecule-1 (ICAM-A) in the Lungs of Silica-Exposed Mice. *Environmental Health Perspectives*. 105(Suppl 5):1183-1190. September. 1997.

Nehls P; Seiler F; Rehn B; Greferath R; Bruch J. Formation and Persistence of 8-Oxoguanine Rat Lung Cells as an Important Determinant for Tumor Formation following Particle Exposure. *Environmental Health Perspectives*. 105(Suppl 5):1231–1240. September. 1997.

Nicholson WJ. Part III. Recent Approaches to the Control of Carcinogenic Exposures. Case Study 1: Asbestos - The TLV Approach. *Annals New York Academy of Science*. 271:152–169. 1976.

Nicholson WJ; Selikoff IJ; Seidman H; Lilis R; Formby P. Long-Term Mortality Experience of Chrysotile Miners and Millers in Thetford Mines, Quebec. *Annals New York Academy of Sciences*. 330:11–21. 1979.

Nikula KJ; Avila KJ; Griffith WC; Mauderly JL. Sites of Particle Retention and Lung Tissue Responses to Chronically Inhaled Diesel Exhaust and Coal Dust in Rats and Cynomolgus Monkeys. *Environmental Health Perspectives*. 105(Suppl 5):1231–1240. September. 1997.

National Institute for Occupational Safety and Health (NIOSH). Method for Determination of Asbestos in Air Using Positive Phase Contrast Microscopy. NIOSH Method 7400. NIOSH, Cincinnati, Ohio, U.S.A. 1985.

National Institute for Occupational Safety and Health (NIOSH). Method for Determination of Asbestos in Air Using Transmission Electron Microscopy. NIOSH Method 7402. NIOSH, Cincinnati, Ohio, U.S.A. 1986.

Oberdorster G. Macrophage-Associated Responses to Chrysotile. *Annals of Occupational Hygiene*. 38(4):601–615. 1994.

Oberdorster G; Morrow PE; Spurny K. Size Dependent Lymphatic Short Term Clearance of Amosite Fibres in the Lung. *Annals of Occupational Hygiene*. 32(Suppl 1):149–156. 1988.

Ollikainen T; Linnainmaa K; Kinnula VL. DNA Single Strand Breaks Induced by Asbestos Fibers in Human Pleural Mesothelial Cells *In Vitro*. *Environmental and Molecular Mutagenesis*. 33(2):153–160. 1999.

Ontario Royal Commission. Report of the Royal Commission on Matters of Health and Safety Arising form the Use of Asbestos in Ontario. Volume 3. 1984.

Osier M; Baggs RB; Oberdörster G. 1997. Intratracheal Instillation vs. Intratracheal Inhalation: Influence of Cytokines on Inflammatory Response. Proceedings of the Sixth International Meeting on the Toxicology of Natural and Man-Made Fibrous and Non-Fibrous Particles. *Environmental Health Perspective*. 105(Suppl 5):1265-1271.

Osornio-Vargas AR; Kalter VG; Badgett A; Hernandez-Rodriguez N; Aguilar-Delfin I; Brody AR. Rapid Communication: Early-Passage Rat Lung Fibroblasts do not Migrate *In Vitro* to Transforming Growth Factor-Beta. *American Journal of Respiratory Cell Molecular Biology*. 8(5):468-471. May. 1993.

Palekar LD; Spooner CM; Coffin DL. Influence of Crystallization Habit of Minerals on *In Vitro* Cytotoxicity. *Annals New York Academy of Sciences*. pp. 673–687. 1979.

Park S-H; Aust AE. Regulation of Nitric Oxide Synthase Induction by Iron and Glutathione in Asbestos-Treated Human Lung Epithelial Cells. *Archives of Biochemistry and Biophysics*. 360(1):47–52. 1998.

Peto J. Lung Cancer Mortality in Relation to Measured Dust Levels in an Asbestos Textile Factory. In *Biological Effects of Mineral Fibres*. Wagner JC (ed.). IARC Scientific Publications. pp. 829–836. 1980a.

Peto J. The Incidence of Pleural Mesothelioma in Chrysotile Asbestos Textile Workers. In *Biological Effects of Mineral Fibres*. Wagner JC (ed.). IARC Scientific Publications. pp. 703–711. 1980b.

Peto J; Doll R; Howard SV; Kinlen LJ; Lewinsohn, HC. A Mortality Study Among Workers in an English Asbestos Factory. *British Journal of Industrial Medicine*. 34:169–173. 1977.

Peto J; Seidman H; Selikoff IJ. Mesothelioma Mortality in Asbestos Workers: Implications for Models of Carcinogenesis and Risk Assessment. *British Journal of Cancer*. 45:124–135. 1982.

Peto J; Doll R; Hermon C; Binns W; Clayton R; Goffe T. Relationship of Mortality to Measures of Environmental Asbestos Pollution in an Asbestos Textile Factory. *Annals of Occupational Hygiene*. 29(3):305–355. 1985.

Pinkerton KE; Brody AR; McLauren DA; Adkins B Jr; O'Connor RW; Pratt PC; Crapo JD. Characterization of the Three Types of Chrysotile Asbestos After Aerosolization. *Environmental Research*. 31:32–35. 1983.

Pinkerton KE; Pratt PC; Brody AR; Crapo JD. Fiber Localization and its Relationship to Lung Reaction in Rats After Chronic Inhalation of Chrysotile Asbestos. *American Journal of Pathology*. 117:484–498. 1984.

Pinkerton KE; Plopper CG; Mercer RR; Rogli VL; Patra AL; Brody AR; Crap JD. Airway Branching Patterns Influence Asbestos Fiber Location and the Extent of Tissue Injury in the Pulmonary Parenchyma. *Laboratory Investigation*. 55(6):688–695. 1986.

Piolatto G; Negri E; LaVecchia C; Pira E; Decarli A; Peto J. An Update of Cancer Mortality Among Chrysotile Asbestos Miners in Balangero, Northern Italy. *British Journal of Industrial Medicine*. 47:810–814. 1990.

Platek SF; Groth DH; Ulrich CE; Stettler LE; Finnell MS; Stoll M. Chronic Inhalation of Short Asbestos Fibers. *Fundamental and Applied Toxicology*. 5:327–340. 1985.

Pooley FD. An Examination of the Fibrous Mineral Content of Asbestos Lung Tissue from the Canadian Chrysotile Mining Industry. *Environmental Research*. 12:281–298. 1976.

Pooley FD. Tissue Burden Studies. In *Short and Thin Mineral Fibres: Identification, Exposure, and Health Effects*. Chatfield EJ (ed). pp. 96–129. 1982.

Pott F. Some Aspects on the Dosimetry of the Carcinogenic Potency of Asbestos and Other Fibrous Dusts. *Staub-Reinhalt*. 38(12):486–490. 1978.

Pott F. Animal Experiments with Mineral Fibers. In *Short and Thin Mineral Fibers: Identification, Exposure, and Health Effects*. Chatfield EJ (ed.). pp. 133–161. 1982.

Pott F; Huth F; Friedrichs KH. Tumorigenic Effect of Fibrous Dust in Experimental Animals. *Environmental Health Perspectives*. 9:313–315. 1974.

Pott F; Huth F; Friedrichs KH. Results of Animal Carcinogenesis Studies After Application of Fibrous Glass and Their Implications Regarding Human Exposure. Occupational Exposure to Fibrous Glass. U.S. HEW Publication No. 76–151. pp. 183–191. 1976.

Pott F; Ziem U; Reiffer RJ; Huth F; Ernst H; Mohr U. Carcinogenicity Studies on Fibres, Metal Compounds, and Some Other Dusts in Rats. *Experimental Pathology.* 32:129–152. 1987.

Raabe O. Deposition and Clearance of Inhaled Particles. In *Occupational Lung Diseases.* Gee JB; et al. (eds.). Raven Press. pp. 1047. 1984.

Quinlan TR; Berube KA; Hacker MP; Taatjes DJ; Timblin CR; Goldberg J; Kimberley P; O'Shaughnessy P; Hemenway D; Torino J; Jimenez LA; Mossman BT. Mechanisms of Asbestos-Induced Nitric Oxide Production by Rat Alveolar Macrophages in Inhalation and *In Vitro* Models. *Free Radical Biology and Medicine.* 24(5):778–788. 1998.

Rahman Q; Mahmood N; Khan SG; Arif JM; Athar M. Mechanism of Asbestos-Mediated DNA Damage: Role of Heme and Heme Proteins. *Environmental Health Perspectives.* 105(Suppl 5):1109–1112. September. 1997.

Roberts DR; Zumwalde RD. Industrial Hygiene Summary Report of Asbestos Exposure Assessment for Brake Mechanics. NIOSH Reports No. IWS-32-4A, Industrial Hygiene Section, NTIS# PB 87-105433. 1982.

Robledo R; Mossman B. Cellular and Molecular Mechanisms of Asbestos-Induced Fibrosis. *Journal of Cellular Physiology.* 180:158–166. 1999.

Roggli VL; Brody AR. Changes in Numbers and Dimensions of Chrysotile Asbestos Fibers in Lungs of Rats Following Short-Term Exposure. *Experimental Lung Research.* 7:133–147. 1984.

Roggli VL; George MH; Brody AR. Clearance and Dimensional Changes of Crocidolite Asbestos Fibers Isolated from Lungs of Rats Following Short-Term Exposure. *Environmental Research.* 42:94–105. 1987.

Rood AP; Scott RM. Size Distributions of Chrysotile Asbestos in a Friction Products Factory As Determined by Transmission Electron Microscopy. *Annals of Occupational Hygiene.* 33(4):583–590. 1989.

Rubino GF; Piolatto GW; Newhouse ML; Scansetti G; Aresini GA; Murray R. Mortality of Chrysotile Asbestos Workers at the Balangero Mine, Northern Italy. *British Journal of Industrial Medicine.* 36:187–194. 1979.

St. George JA; Harkema JR; Hyde DM; Plopper CG. Cell Populations and Structure/Function Relationship of Cells in the Airways. In *Toxicology of the Lung,* 2nd edition. Gardner DE; Crapo JD; McClellan RO (eds.). Raven Press, New York. 1993.

Sanden A; Jarvholm B; Larsson S; Thiringer G. The Risk of Lung Cancer and Mesothelioma After Cessation of Asbestos Exposure: A Prospective Cohort Study of Shipyard Workers. *European Respiratory Journal*. 5:281–285. 1992.

Schnoor T. Unpublished Raw Data Provided to Dr. Wayne Berman by Ms. Terri Schnoor of NIOSH from Study of South Carolina Textile Workers (Dement et al. 1994). 2001.

Sebastien P; Plourde M; Robb R; Ross M. Ambient Air Asbestos Survey in Quebec Mining Towns - Part 1, Methodological Study. Environmental Protection Service, Quebec Region, 3/AP/RQ/1E. pp. 1–41. 1984.

Sebastien P; Plourde M; Robb R; Ross M; Nadon B; Wypruk T. Ambient Air Asbestos Survey in Quebec Mining Towns. Part II: Main Study. Environmental Protection Service, Environment Canada. EPS 5/AP/RQ/2E. July. 1986.

Sebastien P; McDonald JC; McDonald AD; Case B; Harley R. Respiratory Cancer in Chrysotile Textile and Mining Industries: Exposure Inferences from Lung Analysis. *British Journal of Industrial Medicine*. 46:180–187. 1989.

Seidman H. Short-Term Asbestos Work Exposure and Long-Term Observation -- July 1984 Update. Department of Epidemiology, American Cancer Society. 1984.

Seidman H; Selikoff IJ; Hammond EC. Short-Term Asbestos Work Exposure and Long-Term Observation. *Annals New York Academy of Sciences*. 330:61–89. 1979.

Seidman H; Selikoff IJ; Gelb SK. Mortality Experience of Amosite Asbestos Factory Workers: Dose-Response Relationships 5 to 40 Years After Onset of Short-Term Work Exposure. *American Journal of Industrial Medicine*. 10(5/6):479–514. 1986.

Selikoff IJ; Seidman H. Asbestos-Associated Deaths among Insulation Workers in the United States and Canada, 1967–1987. *Annals of the New York Academy of Sciences*. 643:1–14. 1991.

Selikoff IJ; Hammond EC; Seidman H. Mortality Experience of Insulation Workers in the United States and Canada 1943–1976. *Annals New York Academy of Sciences*. 330:91–116. 1979.

Smith DM; Oritiz LW; Archuleta RF; Johnson NF. Long-Term Health Effects in Hamsters and Rats Exposed Chronically to Man-Made Vitreous Fibres. *Annals of Occupational Hygiene*. 34(4B):731–754. 1987.

Snyder J; Virta R; Segreti J. Evaluation of the Phase Contrast Microscopy Method for the Detection of Fibrous and Other Elongated Mineral Particulates by Comparison with a STEM Technique. *American Industrial Hygiene Association Journal*. 48(5):471–477. 1987.

Stanton M; Wrench C. Mechanisms of Mesothelioma Induction with Asbestos and Fibrous Glass. *Journal of the National Cancer Institute*. 48:797–821. 1972.

Stanton M; Layard M; Tegeris A; Miller E; May M; Kent E. Carcinogenicity of Fibrous Glass: Pleural Response in the Rat in Relation to Fiber Dimension. *Journal of the National Cancer Institute*. 58(3):587–597. 1977.

Stanton M; Layard M; Tegeris A; Miller E; May M; Morgan E. Relation of Particle Dimension to Carcinogenicity in Amphibole Asbestos and Other Fibrous Minerals. *Journal of the National Cancer Institute*. 67(5):965–975. 1981.

Stayner L; Smith R; Bailer J; Gilbert S; Steenland K; Dement J; Brown D; Lemen R. Exposure-Response Analysis of Risk of Respiratory Disease Associated with Occupational Exposure to Chrysotile Asbestos. *Occupational and Environmental Medicine*. 54:646–652. 1997.

Stayner LT; Dankovic DA; Lemen RA. Occupational Exposure to Chrysotile Asbestos and Cancer Risk: A Review of the Amphibole Hypothesis. *American Journal of Public Health*. 86(2):176–186. February. 1996.

Stober W; McClellen RO; Morrow PE. Approaches to Modeling Disposition of Inhaled Particles and Fibers in the Lung. In *Toxicology of the Lung*, 2nd edition. Gardner DE; Crapo JD; McClellan RO (eds.). Raven Press, New York. 1993.

Strom KA; Yu CP. Mathematical Modeling of Silicon-Carbide Whisker Deposition in the Lung-Comparison Between Rats and Humans. *Aerosol Science and Technology*. 24(3):193–209. 1994.

Sussman RG; Cohen BS; Lippmann M. Asbestos Fiber Deposition in a Human Tracheobronchial Cast. I. Experimental. *Inhalation Toxicology*. 3:145–160. 1991a.

Sussman RG; Cohen BS; Lippmann M. Asbestos Fiber Deposition in a Human Tracheobronchial Cast. II. Empirical Model. *Inhalation Toxicology*. 3:161–179. 1991b.

Takeuchi T; Nakajima M; Morimoto K. A Human Cell System for Detecting Asbestos Cytogenotoxicity *In Vitro*. *Mutation Research*. 438(1):63–70. 1999.

Tanaka S; Choe N; Hemenway DR; Zhu S; Matalon S; Kagan E. Asbestos Inhalation Induces Reactive Nitrogen Species and Nitrotyrosine Formation in the Lungs and Pleura of the Rat. *Journal of Clinical Investigation*. 102(2):445–454. 1998.

Timblin CR; Guthrie GD; Janssen YWM; Walsh ES; Vacek P; Mossman BT. Patterns of C-Fos and C-Jun Proto-Oncogene Expression, Apoptosis, and Proliferation in Rat Pleural Mesothelial Cells Exposed to Erionite or Asbestos Fibers. *Toxicology and Applied Pharmacology*. 151(1):88–97. 1998a.

Timblin CR; Janssen YMW; Goldberg JL; Mossman BT. GRP78, HSP72/73, and CJUN Stress Protein Levels in Lung Epithelial Cells Exposed to Asbestos, Cadmium or H2O2. *Free Radical Biology & Medicine*. 24(4):632–642. 1998b.

Timbrell V. Deposition and Retention of Fibres in the Human Lung. *Annals of Occupational Hygiene*. 26(1-4):347–369. 1982.

Timbrell V; Hyett AW; Skidmore JW. A Simple Dispenser for Generating Dust Clouds From Standard Reference Samples of Asbestos. *Annals of Occupational Hygiene*. 11:273–281. 1968.

Unfried K; Kociok N; Roller M; Pott F; Dehnen W. P53 mutations in tumours induced by intraperitoneal injection of crocidolite asbestos and benzo[a]pyrene in rats. Experimental Toxicololgoy and Pathology. 49:181-187. 1997.

U.S. EPA (U.S. Environmental Protection Agency). Airborne Asbestos Health Assessment Update. Report 600/8-84-003F, U.S. Environmental Protection Agency. 1986.

U.S. Environmental Protection Agency (EPA). Asbestos Hazard Emergency Response Act: Asbestos-Containing Materials in Schools. Final Rule and Notice (Appendix A: AHERA Method). Federal Register, 40 CFR 763, Vol. 52, No. 2, pp. 41826-41903. October. 1987.

Venzon D; Moolgavkar S. A Method for Computing Profile-likelihood-based Confidence Intervals. *Applied Statistics*. 37:87-94. 1988.

Vincent JH. On the Practical Significance of Electrostatic Lung Deposition of Isometric and Fibrous Aerosols. *Journal Aerosol Science*. 16(6):511–519. 1985.

Vincent JH; Johnston AM; Jones AD; Bolton RE; Addison J. Kinetics of Deposition and Clearance of Inhaled Mineral Dusts During Chronic Exposure. *British Journal of Industrial Medicine*. 42:707–715. 1985.

Wagner JC. Opening Discussion -- Environmental and Occupational Exposure to Natural Mineral Fibres. In *Biological Effects of Mineral Fibres*. Wagner JC (ed.). IARC Scientific Publications. pp. 995–998. 1980.

Wagner JC; Berry G; Skidmore JW; Timbrell V. The Effects of the Inhalation of Asbestos in Rats. *British Journal of Cancer*. 29:252–269. 1974.

Wagner JC; Berry G; Skidmore JW. Studies of the Carcinogenic Effects of Fiber Glass of Different Diameters Following Intrapleural Innoculation in Experimental Animals. NIOSH 76-151. pp.193–197. 1976.

Wagner JC; Berry G; Hill R; Munday D; Skidmore J. Animal Experiments with MMM(V)F - Effects of Inhalation and Intrapleural Inoculation in Rats. In *Biological Effects of Man-Made Fibres -- Proceedings of a WHO/IARC Conference*, Copenhagen. pp. 209–233. 1982.

Wagner JC; Skidmore JW; Hill RJ; Griffith DM. Erionite Exposure and Mesotheliomas in Rats. *British Journal of Cancer*. 51:727–730. 1985.

Wagner JC; Griffiths DM; Munday DE. Experimental Studies with Palygorskite Dusts. *British Journal of Industrial Medicine*. 44(11):749–763. 1987.

Walker AM. Declining Relative Risks for Lung Cancer After Cessation of Asbestos Exposure. *Journal of Occupational Medicine*. 26(2):422–426. 1984.

Walton WH. The Nature, Hazards, and Assessment of Occupational Exposure to Airborne Asbestos Dust: A Review. *Annals of Occupational Hygiene*. 25:117–247. 1982.

Warheit DB; Snajdr SI; Hartsky MA; Frame SR. Lung Proliferative and Clearance Responses to Inhaled para-Aramid RFP in Exposed Hamsters and Rats: Comparisons with Chrysotiles Asbestos Fibers. *Environmental Health Perspectives*. 105(Suppl 5):1219–1222. September. 1997.

Weill H. 1994. Cancer Mortality in Chrysotile Mining and Milling: Exposure-Response. Asbestos-Cement. *Annals of Occupational Hygiene*. 38(4):412. 1994.

Weill H; Hughes J; Waggenspack C. Influence of Dose and Fibre Type on Respiratory Malignancy Risk in Asbestos Cement Manufacturing. *American Review of Respiratory Disease*. 120:345–354. 1979.

Wilks SS. Mathematical Statistics. 2nd edition. Wiley Publication, New York. 1963.

Winer AA; Cossette M. The Effect of Aspect Ration on Fiber Counts: A Preliminary Study. *Annals New York Academy of Sciences*. 330:661–672. 1979.

Weitzman SA; Graceffa P. Communication: Asbestos Catalyzes Hydroxyl and Superoxide Radical Generation from Hydrogen Peroxide. *Archives of Biochemistry and Biophysics*. 228(1):373–376. 1984.

World Health Organization (WHO). Reference Methods for Measuring Airborne Man-Made Mineral Fibers (MMMF). 1985.

Wright GW; Kuschner M. The Influence of Varying Lengths of Glass and Asbestos Fibres on Tissue Response in Guinea Pigs. In *Inhaled Particles: Part 2*. Walton WH; McGovern B (eds.). Pergamon Press Oxford. pp. 455–474. 1975.

Wylie AG; Virta RL; Segretti JM. Characterization of Mineral Population by Index Particle: Implications for the Stanton Hypothesis. *Environmental Research*. 43:427–439. 1987.

Wylie AG; Bailey KF; Kelse JW; Lee RJ. The Importance of Width in Asbestos Fiber Carcinogenicity and its Implications for Public Policy. *American Industrial Hygiene Association Journal*. 54:239–252. 1993.

Wylie AG; Skinner HCW; Marsh J; Snyder H; Garzione C; Hodkinson D; Winters R; Mossman BT. Mineralogical Features Associated with Cytotoxic and Proliferative Effects of Fibrous Talc and Asbestos on Rodent Tracheal Epithelial and Pleural Mesothelial Cells. *Toxicology and Applied Pharmacology*. 147:143–150. 1997.

Yamaguchi R; Hirano T; Ootsuyama Y; Asami S; Tsurudome Y; Fukada S; Yamato H; Tsuda T; Tanaka I; Kasai H. Increased 8-Hydroxyguanine in DNA and Its Repair Activity in Hamster and Rat Lung After Intratracheal Instillation of Crocidolite Asbestos. *Japanese Journal of Cancer Research.* 90(5):505–509. 1999.

Yamate G; Agarwal SC; Gibbons RD. Methodology for the Measurement of Airborne Asbestos by Electron Microscopy. U.S. EPA Report No. 68-02-3266. U.S. Environmental Protection Agency, Washington, D.C., U.S.A. 1984.

Yeh H-C; Harkema JR. Gross Morphometry of Airways. In *Toxicology of the Lung*, 2nd edition. Gardner DE; Crapo JD; McClellan RO (eds.). Raven Press, New York. 1993.

Yu CP; Asgharian B. A Kinetic Model of Alveolar Clearance of Amosite Asbestos Fibers from the Rat Lung at High Lung Burdens. *Journal of Aerosol Science.* 21:21–27. 1990b.

Yu CP; Yoon KJ. Investigator's Report: Retention Modeling of Diesel Exhaust Particles in Rats and Humans. 1991.

Yu CP; Asgharian B; Abraham JL. Mathematical Modeling of Alveolar Clearance of Chrysotile Asbestos Fibers from the Rat Lungs. *Journal of Aerosol Science.* 21:587–594. 1990a.

Yu CP; Asgharian B; Pinkerton KE. Intrapulmonary Deposition and Retention Modeling of Chrysotile Asbestos Fibers in Rats. *Journal of Aerosol Science.* 22(6):757–761. 1991.

Yu CP; Zhang L; Oberdoster G; Mast RW; Glass LR; Utell MJ. Deposition Modeling of Refractory Ceramic Fibers in the Rat Lung. *Journal of Aerosol Science.* 25(2):407–417. 1994.

Yu CP; Zhang L; Oberdoster G; Mast RW; Maxim D; Utell MJ. Deposition of Refractory Ceramic Fibers (RCF) in the Human Respiratory Tract and Comparison with Rodent Studies. *Aerosol Science and Technology.* 23(3):291–300. 1995a.

Yu CP; Zhang L; Oberdoster G; Mast RW; Glass LR; Utell MJ. Clearance of Refractory Ceramic Fibers (RCF) from the Rat Lung - Development of a Model. *Environmental Research.* 65(2):243–253. 1995b.

Zalma R; Bonneau L; Guignard J; Pezerat H; Jaurand M-C. Formation of Oxy Radicals by Oxygen Reduction Arising from the Surface Activity of Asbestos. *Canadian Journal of Chemistry.* 65:2338–2341. 1987.

Zanella CL; Timblin CR; Cummins A; Jung M; Goldberg J; Raabe R; Tritton TR; Mossman BT. Asbestos-Induced Phosphorylation of Epidermal Growth Factor Receptor is Linked to c-fos and apoptosis. *American Journal of Physiology.* 277(4:Part 1):L684–L693. 1999.

Zhang Y; Lee TC; Guillemin B; Yu M-C; Rom WN. Enhanced IL-1Beta and Tumor Necrosis Factor-Alpha Release and Messenger RNA Expression in Macrophages from Idiopathic Pulmonary Fibrosis or After Asbestos Exposure. *Journal of Immunology.* 150(9):4188–4196. May. 1993.

Zhu S; Manuel M; Tanaka S; Choe N; Kagan E; Matalon S. Contribution of Reactive Oxygen and Nitrogen Species to Particulate-Induced Lung Injury. *Environmental Health Perspectives.* 106(5):1157–1163. 1998.

Zoitus BK; De Meringl A; Rouyer E; Thelohan S; Bauer J; Law B; Boymel PM; Olson JR; Christensen VR; Guldberg M; Koenig AR; Perander M. *In Vitro* Measurement of Fiber Dissolution Rate Relevant to Biopersistence at Neutral pH: An Interlaboratory Round Robin. *Inhalation Toxicology.* 9:525–540. 1997.

APPENDIX A: UPDATE OF POTENCY FACTORS FOR LUNG CANCER (K_L) AND MESOTHELIOMA (K_M)

Estimates of risk of dying of lung cancer or mesothelioma from asbestos exposure are quantified by means of mathematical models that express risk as a function of exposure. The models utilized in the 1986 U.S. EPA Airborne Asbestos Health Assessment Update (U.S. EPA 1986) contain parameters (K_L for lung cancer and K_M for mesothelioma) that gauge the potency of asbestos for causing these health effects. USEPA calculated K_L and K_M values from a number of studies. In this section these K_L and K_M calculations are revised using the same models as in the U.S. EPA (1986) update, but incorporating newer data from more recent publications. Since the 1986 update, additional cohorts have been studied from several new exposure settings and the followup periods have been extended for several of the previously studied cohorts.

In the 1986 update, K_M values were not calculated from all of the available studies, perhaps owing to the limited number of mesotheliomas observed in some of these studies. In this update, an attempt has been made to utilize any study with suitable health and exposure data, regardless of the number of mesotheliomas reported, and to quantify the statistical uncertainty attributable to small numbers using statistical confidence limits. Since the present work utilizes somewhat different methods from the 1986 update, for consistency, all of the K_L and K_M values were recalculated, even from studies for which no new data were available. Table A-1 contains a summary of the new values for K_L and Table A-2 contains the new values for K_M. The original values from the 1986 update are also provided for comparison. These tables also contain statistical confidence limits and ad hoc "uncertainty limits" for K_L and K_M. The derivation of these limits will be described in detail in subsequent sections.

A.1 LUNG CANCER MODEL

The 1986 U.S. EPA lung cancer model (U.S. EPA 1986) assumes that the relative risk, RR, of mortality from lung cancer at any given age is a linear function of cumulative asbestos exposure (fiber-years/ml, or f-y/ml, as measured by PCM), omitting any exposure in the most recent 10 years. This exposure variable is denoted by CE_{10}. The 10-year lag embodies the assumption that exposures during the most recent 10 years do not affect current lung cancer mortality risk. The mathematical expression for this model is

$$RR = 1 + K_L * CE_{10}, \qquad \text{(Eq. A-1)}$$

where the linear slope, K_L, is the "lung cancer potency factor." To make allowance for the possibility that the background lung cancer risk in the exposed population differs from that of the comparison population, the model is expanded to the form,

$$RR = \alpha * (1 + K_L * CE_{10}). \qquad \text{(Eq. A-2)}$$

With this form of the model the relative risk at zero exposure is α rather than 1.0. Both K_L and α are estimated by fitting the model to data. The type of data usually available for applying this model are from cohort studies in which observed and expected (based on an appropriate comparison population, e.g., U.S. males) numbers of lung cancers are categorized by cumulative exposure incorporating a 10 year lag. To explore the adequacy of the model, it is useful to have the data cross-classified by one or more other variables, such as latency.

Frequently the cumulative exposure variable available from the published report of a study does not incorporate a lag (or, less frequently, incorporates a lag of less than 10 years). In this report, rather than attempting an ad hoc correction, no correction for lag has been made. Although this tends to cause K_L values to be slightly underestimated, this is unlikely to be a serious problem. For most cohorts, exposures decreased significantly over time. Also, in many studies, followup didn't begin until several years after the start of exposure and the bulk of the lung cancers occurred at older ages. All of these factors tend to mitigate the error created from use of data with no lag. Moreover, use of an ad hoc correction for lag could hinder comparisons of K_L values among studies that do not employ a lag (which includes the majority of studies).

A.2 MESOTHELIOMA MODEL

The 1986 U.S. EPA mesothelioma model (U.S. EPA 1986) can be derived by assuming that the mortality rate at time t after the beginning of exposure can be calculated by summing the contributions from exposure at each increment of time, du, in the past. The contribution to the mortality rate at time t from exposure to E(u) f/ml (as measured by PCM) at time u is assumed to be proportional to the product of the exposure rate, E(u), and $(t-u-10)^2$, the square of the elapsed time minus a lag of 10 years. Thus, as with the lung cancer model, the mesothelioma model assumes a 10-year lag before exposure has any effect upon risk. With the additional assumption that the background rate of mesothelioma is zero, the mesothelioma mortality rate at time t since the beginning of exposure is given by

$$I_M(t) = 3 * K_M * \int_0^{t-10} E(u) * (t - u - 10)^2 du, \qquad \text{(Eq. A-3)}$$

where t and u are in years, and $I_M(t)$ is the mortality rate per year at year t after the beginning of exposure. The proportionality factor, K_M, is called the "mesothelioma potency factor." The factor of "3" is needed to retain the same meaning of K_M as defined by U.S. EPA (1986).

If exposure is at a constant level, E, for a fixed duration, DUR, this model can be written as

$$I_M(t) = \begin{cases} 0 & 0 \le t \le 10 \\ K_M * E * (t - 10)^3 & 10 \le t \le 10 + DUR \\ K_M * E * [(t - 10)^3 - (t - 10 - DUR)^3] & DUR \le t \end{cases} \qquad \text{(Eq. A-4)}$$

The genesis of this model and its agreement with data were discussed in U.S. EPA (1986).

Through the courtesy of Dr. Corbett McDonald, Professor Douglass Liddell, Dr. Nicholas de Klerk, Dr. John Dement, and the National Institute for Safety and Health (NIOSH), raw data on mesothelioma mortality were obtained from a cohort of Quebec chrysotile miners and millers

(Liddell et al. 1997; McDonald et al. 1980a), a cohort of Wittenoom, Australia crocidolite miners and millers (Armstrong et al. 1988; de Klerk et al. 1994), and a cohort of workers from a plant in Charleston, South Carolina that manufactured textiles from chrysotile (Dement et al. 1983a,b, 1994; Dement and Brown 1998). These data were used to calculate K_M values in a more accurate manner for these cohorts (using the "exact" approach described below) and to explore the potential magnitude of the errors incurred by the crude application of cohort-wide averages when fitting the mesothelioma model.

A.3 STATISTICAL FITTING METHODS

The method of maximum likelihood (Cox and Oakes 1984; Venzon and Moolgavkar 1988) was used herein to fit the lung cancer and mesothelioma models to data and to estimate K_L and K_M. The profile likelihood method was used to calculate statistical confidence intervals and likelihood ratio tests were used to assess goodness-of-fit and test hypotheses.

Typically the data for calculating a lung cancer potency factor, K_L, consist of observed and expected (based on an external control group, such as U.S. males) numbers of cancer deaths categorized by cumulative exposure. The likelihood of these data is determined by assuming that the deaths in different exposure categories are independent and that the number of deaths in a particular category has a Poisson distribution with expected number given by the expected number predicted by the external control group times the relative risk given by either expression (Eq. A-1 or A-2).

In the typical situation, the published data most useful for calculating the mesothelioma potency factor, K_M, consist of the number of mesothelioma deaths and person-years of observation categorized by time since first exposure. The likelihood of these data is determined by assuming statistical independence of the number of mesothelioma deaths in different categories and that the number of mesothelioma deaths in a category has a Poisson distribution with mean equal the number of person-years in the category times expression (Eq. A-4), using average values for E, DUR, and t appropriate for that category.

The fitting of the mesothelioma model (Eq. A-3) to raw (unsummarized) mesothelioma data is accomplished using an "exact" maximum likelihood method. The cumulative mesothelioma hazard is defined as

$$H(t) = \int_0^t I_M(u)\, du. \qquad \text{(Eq. A-5)}$$

The contribution to the likelihood of a person whose followup terminated at t is $S(t) = \exp[\, -H(t)\,]$ if the followup did not terminate in death from mesothelioma, and $I_M(t) * S(t)$ if the person died of mesothelioma. The complete likelihood was defined as the product of these individual contributions. The integrals in expressions (Eq. A-3 and A-5) were evaluated numerically.

A.4 SELECTION OF A "BEST ESTIMATE" OF K_L AND K_M

For each study for which a K_L or K_M is estimated, a "best estimate" is provided. For lung cancer, the best estimate of K_L (Table A-1) was generally assumed to be the maximum likelihood estimate (MLE) obtained with α estimated. For mesothelioma, the best estimate of K_M (Table A-2) is generally the maximum likelihood estimate derived from the best-fitting model in the form (Eq. A-3) for raw data and (Eq. A-4) for published data. As described in the descriptions of the individual studies, in a few cases these general rules had to be adapted to fit the particular form of the data available.

A.5 UNCERTAINTY IN K_L AND K_M

Statistical uncertainty in K_L and K_M estimates is expressed using 95% upper and lower statistical confidence limits. These limits (summarized in Table A-1 for lung cancer and Table A-2 for mesothelioma) were computed using the profile likelihood method and (for K_L) with α estimated.

However, non-statistical sources of uncertainty, such as model uncertainty and uncertainty in exposure, are also likely to be very important. Although these uncertainties are difficult to quantify, it is important to attempt quantification, since presentation of statistical uncertainty alone may provide a misleading picture of the reliability of the estimates. Consequently, an ad hoc approach to quantifying non-statistical uncertainty was adopted in this report. In this approach, the primary sources of uncertainty are identified. Then, for each study, a factor was selected for each uncertainty source using guidelines that will be described in this appendix. The individual factors were combined with the statistical confidence bounds to arrive at an "uncertainty range" for K_L or K_M for each particular cohort. These ranges are described in detail in following sections and are summarized in Table A-1 for lung cancer and Table A-2 for mesothelioma.

Because the most serious uncertainties among published epidemiology studies are often attributable to the estimation of exposure, three factors (F1, F2, and F3) were defined to address distinct sources of uncertainty associated with exposure. Two additional factors (F4L and F4M) were defined to account for uncertainty due to special limitations that had to be addressed to facilitate estimation of exposure-response factors from specific studies for lung cancer and mesothelioma, respectively.

To define the factors we used to address uncertainty associated with exposure, we first considered that, ideally, cumulative exposure would be estimated in an epidemiology study by:

- continuously monitoring the concentrations to which the worker is exposed over their entire working life;
- measuring such concentrations using personal monitors (samplers worn by workers with sampling ports placed within a few inches of the breathing zone of the worker); and

- analyzing samples in a manner appropriate for determining the concentration of the specific range of structures of interest[1].

In practice, however, measurements are collected only periodically at fixed locations considered representative of worker exposures for jobs performed at that location (local operations). Moreover, measurements were frequently derived using analytical methods that report results in units different from those of interest, so that some type of conversion is required. Then, typically, cumulative exposures are estimated for individual workers as the sum (over the set of jobs held by that worker) of the product of the mean exposure concentration for each job and the duration over which that job is performed. Thus:

$$\overline{C}_{PCM_i} = Q\sum_j C_{LO}D_i \qquad \text{(Eq. A-6)}$$

where:

$\overline{C}_{PCM}$ is the cumulative exposure experienced by a worker to PCM fibers (f-years/ml);

Q is a factor used to convert concentration measurements in a particular study to PCM fiber concentrations whenever the measurements in the study were collected using a different method (usually dust concentrations determined by midget impinger, in which case the units of Q are f/ml/mppcf);

C_{LO} is the concentration estimated for a particular "local operation" typically derived by a combination of measurement and extrapolation; and

D_j is the duration of time that the worker spent working in local operation "j".

Note that, because exposure concentrations at specific locations have generally been observed to decrease over time due to changes in process, introduction of dust control equipment, and other factors, cumulative annual exposures are generally estimated for workers in the manner described above and the annual exposures are then summed. However, this does not change the general applicability of Equation A-6.

Based on Equation A-6, a factor, F1, is defined to account for uncertainty introduced in the manner that the C_{LO} are determined in specific epidemiology studies; a factor, F2, is used to address uncertainty associated with the determination of the conversion factors, Q, for specific studies; and F3 is defined to represent uncertainty in the manner that job matrices are developed

[1]Most comparisons of epidemiology studies involve converting estimates of cumulative exposures to fiber concentrations as determined by phase contrast microscopy (PCM) using the "membrane filter method". Thus, for the discussion above, the range of structures (exposure index) of interest would be those determined using the membrane filter method. Importantly, however, discussions in other portions of this document deal with determining asbestos concentrations using an exposure index representing the specific range of structures that contribute directly to biological activity, which should not be confused with the exposure index reported using the membrane filter method.

in specific studies to assign workers to specific local operations over specific durations. The manner in which values were assigned for each uncertainty factor is described more fully below.

A.5.1 The Factor F1

As indicated above, the factor, F1, represents the uncertainty in concentration estimates to which workers are exposed (in whatever units of exposure that are reported in a particular study). In addition to analytical uncertainty, considerations addressed when assigning values for F1 for specific epidemiology studies include:

- to what extent exposure concentrations were directly determined from measurements collected at the locations and times that worker exposures actually occurred; and

- whether measurements were derived from personal monitoring or from area monitoring (sampling a general area that is assumed representative of exposure conditions associated with jobs performed within the local area).

Regarding the latter consideration, exposure concentrations estimated in the published epidemiology studies were almost universally determined by area, rather than personal monitoring. As has been reported in several of these studies (see, for example, McDonald et al. 1983b), area monitoring can miss short-term, high-level exposures contributed by the personal actions being performed by a worker. Moreover, certain periodic activities potentially associated with extremely high exposure (typically involving cleanup) were not performed during time periods when work areas were routinely monitored.

Regarding the first bullet above, published epidemiology studies differ in the frequency and time period over which sampling was conducted. With few exceptions, little or no sampling was conducted prior to the 1950's when exposure concentrations are thought generally to be higher than those monitored more recently, due to lack of use of dust control equipment and procedures that were introduced only later. For many studies, therefore, early exposures had to be estimated by extrapolation from later measurements and the care with which such extrapolations were performed also varies from study to study.

Studies vary in the degree to which the range of local operations associated with a particular facility were individually sampled. Exposure conditions attendant to jobs performed in association with local operations not sampled directly would then be extrapolated from measurements collected for other local operations assumed to be associated with "comparable exposures." As with extrapolations in time, the care with which such spatial extrapolations were performed varies from study to study.

Values assigned for F1 vary between 1.5 and 4 (all to the nearest 0.5). The most typical value assigned is 2.0 for studies in which additional uncertainty is introduced due to use of area samplers rather than personal samplers, lack of measurements representative of episodic but high-exposure jobs (usually associated with cleanup), and lack of direct measurements from the earliest periods of exposure (when dust control equipment and procedures were absent). To be assigned a value of 2.0, however, authors must have had access to substantial numbers of

samples representative of the majority of the local operations of interest, must have described a systematic procedure for extrapolating exposure estimates to less well studied local operations, and must have described a systematic procedure for extrapolating exposure estimates to earlier times when measurements were lacking. The logic used to assign F1 values (and values for the other uncertainty factors) for individual studies is described for each study in Section A.6 of this appendix.

A.5.2 The Factor F2

F2 is a factor used to characterize the uncertainty introduced in deriving conversion factors to convert from the exposure indices measured in a particular study to the exposure index typically reported using the membrane filter method (as determined by PCM). In about half of the studies, concentrations are estimated in millions of dust particles per cubic foot (mppcf) as determined by midget impinger (see Section 4.3). The uncertainty introduced by such conversions varies from study to study because:

- for a small number of studies, the majority of measurements were performed by the membrane filter method so that conversion was unnecessary;
- for some studies, conversion factors were derived from a statistical analysis of a set of side-by-side measurements determined, respectively, using the membrane filter method and the other method from which measurements need to be converted (typically the midget impinger method);
- for some studies, lack of side-by-side measurements required expert judgement for comparing across samples collected at different times and locations; and
- for some studies, conversion factors were not derived at all, but were adapted from other studies of similar processes.

Moreover, as has been demonstrated in several studies, the factors used to convert other measurements (primarily midget impinger) to the exposure index determined by PCM vary as a function of study environment, local operation, and time. For example, the ratio of PCM to midget impinger derived from side-by-side measurements in a single study reportedly varied between 0.3 and 30 (McDonald et al. 1980a).

Note that, given the above, the factors used to convert measured concentrations to exposure concentrations in units of interest (Q in Equation A-6) ideally should be brought into the sum on the right and determined individually for each local operation. However, with the exception of the South Carolina study by Dement and coworkers (Dement et al. 1994; Dement and Brown 1998), only average (study-wide) conversion factors are typically estimated in any particular study.

Values for F2 assigned to particular studies vary between 1.0 and 3.0. Studies in which conversions were not required (due to routine use of PCM) or studies in which conversion factors were determined for specific operations were assigned an F2 value of 1.0. Studies in which a study-wide conversion factor was determined from paired measurements are assigned a

value of 1.5. Studies in which conversion factors were adapted from other studies or for which authors did not define a conversion factor were assigned larger values for F2.

A.5.3 The Factor F3

The factor, F3, is used in this study to represent the uncertainty attributable to the manner in which job-exposure matrices were constructed in the various published epidemiology studies. Authors for some studies had detailed work histories that could be used to identify the complete set of specific jobs that each worker performed over their working life and the duration of time spent on each job. Authors from other studies did not have access to individual work histories so that crude estimates of average duration was applied to all members of the cohort. The factor, F3, is used to account for conditions in which less than optimal job histories were used to identify the set of jobs performed by each worker and the duration that each worker spent performing each such job.

A.5.4 The Factor F4L for Lung Cancer and F4M for mesothelioma

An additional factor is included (F4L for lung cancer) and (F4M for mesothelioma) to account for uncertainties in mortality data (e.g., when diagnosis is uncertain for a substantial fraction of potential mesothelioma cases) or when approximations or assumptions are required because the data are not presented in the form needed for fitting the exposure-response models. Two assigned F4L values are greater than 1.0 (1.5 and 2.0), and six F4M values are greater than 1.0; these six values range from 2.0 to 5.0.

A.5.5 Combining Individual Uncertainty Factors into an Overall "Uncertainty Range"

As indicated above, in addition to statistical confidence intervals, four uncertainty factors have been proposed: F1: exposure, general; F2: exposure conversion factor; F3: lack of individual work histories; and F4L (lung cancer) and F4M (mesothelioma): non-exposure related. Since it is unlikely that all of the uncertainty sources would cause errors in the same direction in the same study, rather than multiplying the uncertainty factors, an overall uncertainty factor, F, was calculated as:

$$F = \exp\{ [\mathrm{Ln}^2(F1) + \mathrm{Ln}^2(F2) + \mathrm{Ln}^2(F3) + \mathrm{Ln}^2(F4)]^{1/2} \},$$

where 1.0 is the default value for any factor not explicitly provided. The overall "uncertainty range" for K_L or K_M was calculated by dividing the statistical 95% lower bound by F and multiplying the 95% upper bound by F.

A.6 ANALYSIS OF INDIVIDUAL EPIDEMIOLOGY STUDIES

Predominately Chrysotile Exposure

Quebec Mines and Mills. Liddell et al. 1997 extended the followup into 1992 of a cohort of about eleven thousand workers at two chrysotile asbestos mines and related mills in Quebec that had been studied earlier by McDonald et al. 1980b (follow-up through 1975) and McDonald et al. 1993 (follow-up through 1988). Production at the mines began before 1900. The cohort

consisted of workers who worked ≥1 month and who were born between the years of 1891 and 1920. Follow-up began for each individual after 20 years from first employment. The most recent follow-up (Liddell et al. 1997) traced 9,780 men through May 1992, whereas 1,138 (10%) were lost to view, most of whom worked for only a few months prior to 1935. Of those traced, 8,009 (82%) were deceased as of 1992.

Estimates of dust levels in specific jobs were made from some 4,000 midget impinger measurements collected systematically starting in 1948 and periodically in the factory beginning in 1944. Estimates for the period prior to 1949 utilized interviews with long-term employees and comparison with more recent conditions. These dust-level estimates were matched to individual job histories to produce estimates of cumulative exposure for each worker (mppcf-years). Conversions between dust levels and PCM concentrations were derived from side-by-side samples. On the basis of over 600 side-by-side midget impinger and optical microscopy measurements, it was estimated that 3.14 fibers/ml was, on the average, equivalent to 1.0 mppcf (McDonald et al. 1980b).

Liddell et al. (1997) categorized cancer deaths after age 55 from of lung, trachea, and bronchus by cumulative asbestos exposure to that age (Liddell et al. 1997, Table 8). Standardized mortality ratios (SMRs) were calculated based on Quebec rates from 1950 onward, and Canadian, or a combination of Canadian and Quebec rates, for earlier years. Table A-4 shows the fit of the lung cancer model to these data. Although the models both with $\alpha=1$ and α variable provided reasonably adequate fits to the data, the hypothesis $\alpha=1$ can be rejected ($p=0.014$). The model with α estimated yields a best estimate of K_L of 0.00029 $(\text{f-y/ml})^{-1}$, 90% CI: (0.00019, 0.00041). With $\alpha=1$, the estimate was $K_L=0.00041$ $(\text{f-y/ml})^{-1}$, 90% CI: (0.00032, 0.00051).

Smoking history was obtained in 1970 by a questionnaire administered to current workers, and to proxies of those who had died after 1950. Although no analyses of lung cancer and asbestos exposure were presented for the 1992 follow-up (Liddell et al. 1997) that controlled for smoking, such an analysis was conducted for the follow-up that continued through 1975 (McDonald et al. 1980a). Table 9 of McDonald et al. (1980a) contained data on lung cancer categorized jointly by cumulative exposure to asbestos and by smoking habit. Two models were fit to these data: the multiplicative model for relative risk

$$RR = \alpha * (1 + b * d) * (1 + c * x),$$

and the additive model

$$RR = \alpha * (1 + b * d + c * x),$$

where d is cumulative exposure to asbestos to age 45, x is number of cigarettes smoked per day, and α,b, and c are parameters estimated from the data. The multiplicative model fit the data well, but the fit of the additive model was inadequate. This corroborates the multiplicative interaction between smoking and asbestos exposure in causing lung cancer (Hammond et al. 1979). The estimate of potency using the multiplicative model was 0.00051 $(\text{f-y/ml})^{-1}$, which was very close to that of 0.00045 $(\text{f-y/ml})^{-1}$ estimated from Table 5 of McDonald et al. (1980a), which did not utilize smoking data. This suggests that the association between lung cancer and asbestos exposure is not strongly confounded with smoking in this cohort.

By 1993, 38 deaths from mesothelioma had occurred in this cohort (Liddell et al. 1997). Through the courtesy of Dr. Corbett McDonald and Professor Douglass Liddell, the underlying mesothelioma data from this study were provided for additional analysis (Liddell 2001). These data contained the following information on each worker: the date of birth, asbestos exposure history, last date of follow-up, whether follow-up ended as a result of death from mesothelioma, location of first employment, and whether a worker had been employed at more than one location.

Nine distinct locations for first employment were coded. Locations 5–9 referred to small operations, some having very heterogeneous exposures, and were omitted from the analysis. Also, workers who worked at more than one location were omitted. After these exclusions, there remained 9,244 workers who worked at Locations 1–4, and among whom 35 deaths from mesothelioma occurred. Location 1 (4,195 men, 8 deaths from mesothelioma) was the mine and mill at the town of Asbestos. Location 2 (758 men, 5 deaths) was a factory at the town of Asbestos that, in addition to processing chrysotile, had also processed some crocidolite. Location 3 (4,032 men, 20 deaths) comprised a major mining and milling company complex near Thetford Mines. Location 4 (259 men, 2 deaths) comprised a number of smaller mines and mills also in the vicinity of Thetford Mines. Because of the small number of workers at Location 4, the fact that both locations were near Thetford Mines, and the fact that the separate K_M values obtained from Locations 3 and 4 were similar, data from these locations were combined. The remaining groups were analyzed separately, because of the crocidolite used at Location 2, and because of evidence of greater amounts of tremolite in the ore at Thetford Mines that at Asbestos (Liddell et al. 1997).

The availability of the raw data from this study made it possible calculate K_M from this study using an "exact" likelihood approach based on expression (Eq. A-3) that did not involve any grouping of data, or use of average values. For Location 1 (Asbestos mine and mill), $K_M=0.013\times10^{-8}$, 90% CI: (0.0068×10^{-8}, 0.022×10^{-8}). For Location 2 (Asbestos factory), $K_M=0.092\times10^{-8}$, 90% CI: (0.040×10^{-8}, 0.18×10^{-8}). For Locations 3 and 4, $K_M= 0.021\times10^{-8}$, 90% CI: (0.014×10^{-8}, 0.029×10^{-8}). The K_M estimate from Location 1 (whose ore was reported to have a lower tremolite content) was about one-half that from Locations 3 and 4, although this difference was not significant ($p=0.22$). The K_M estimated from Location 2, the mill where substantial crocidolite was used, was 4–7 times higher than the K_L estimated from Location 1 and Locations 3 and 4.

For comparison purposes, K_M were also calculated using grouped data and applying expression (4), since this is the method that must be used with most studies. For Location 1 (3 and 4) the K_M estimate based on the "exact" analysis was 34% (25%) higher than that based upon grouped data. This suggests that reliance upon published data for calculating K_M may introduce some significant errors in some cases. Such errors may be further compounded by the failure of some studies to report the needed data on levels and durations of exposure in different categories of time since first exposure.

For this study F1 is set equal to 2.0. This study is the paradigm used to define the typical case (see Section A.5.1) in which increased uncertainty can be attributed to use of area rather than personal samplers, lack of measurements early in the study, and lack of direct measurements from certain episodic but high-exposure operations. At the same time, the authors of this study

appear to have used the available data in a systematic and objective manner to address the issues raised by the lack of sampling.

The uncertainty factor F2 is set equal 1.5 for this study to reflect use of a conversion factor that is derived from paired samples, but that is based on a project wide average, rather than addressing variation for specific, local operations.

All other uncertainty factors are set equal to 1.0 for this study due to lack of remarkable distinctions. Thus:

F1 = 2.0
F2 = 1.5
F3 = 1.0
F4L = 1.0
F4M = 1.0

These uncertainty factors, when coupled with the statistical confidence limits, resulted in the uncertainty ranges for K_L and K_M shown in Tables A-1 and A-2.

Italian Mine and Mill. Piolatto et al. (1990) conducted additional follow-up of workers at a chrysotile mine and mill in Italy that was earlier studied by Rubino et al. (1979). The cohort consisted of 1058 workers with at least 1 year of employment between 1946 and 1987. Follow-up extended from 1946 through 1987, which is 12 more years of follow-up than in Rubino et al. (1979). Lung cancer mortality was compared to that of Italian men.

As described in Rubino et al. (1979), fiber levels were measured by PCM in 1969. In order to estimate earlier exposures, information on daily production, equipment changes, number of hours worked per day, etc. were used to create conditions at the plant during earlier years. PCM samples were obtained under these simulated conditions and combined with work histories to create individual exposure histories.

Piolatto et al. (1990) observed 22 lung cancers compared to 11 in the earlier study (Rubino et al. 1979). Lung cancer was neither significantly in excess nor significantly related to cumulative asbestos exposure. Piolatto et al. (1990, Table 1) presented observed and expected lung cancers (based on age- and calendar-year-specific rates for Italian men) categorized by cumulative exposure in f-y/ml. The lung cancer model with fixed α provided a good fit to these data (Table A-5, p=0.75) and allowing α to vary did not significantly improve the fit. The K_L estimate with α=1 was 0.00035 $(\text{f-y/ml})^{-1}$, with 90% CI: (0, 0.0015). With α allowed to vary the estimate was K_L=0.00051 $(\text{f-y/ml})^{-1}$ with 90% CI: (0, 0.0057).

Two mesotheliomas were observed by Piolatto et al. (1990), compared to one found by Rubino et al. (1979). However, data were not presented in a form from which K_M could be estimated.

Regarding uncertainty factors, F1 is assigned a value 2.0 for this study for reasons similar to those described for Quebec. F2 is assigned a value of 1.0 because measurements were conducted using PCM so that conversion is unnecessary for this study. All other factors are also assigned a value of 1.0 because there are no other unique limitations. Thus:

F1 = 2.0
F2 = 1.0
F3 = 1.0
F4L = 1.0

These uncertainty factors, when coupled with the statistical confidence limits, resulted in the uncertainty range for K_L shown in Table A-1.

Connecticut Friction Product Plant. McDonald et al. (1984) evaluated the mortality of workers employed in a Connecticut plant that manufactured asbestos friction products. The plant began operation in 1913 and used only chrysotile until 1957, when a little anthophyllite was used. Also, a small amount of crocidolite (about 400 pounds) was handled experimentally between 1964 and 1972. Brake linings and clutch facings were made beginning in the 1930s, and production of automatic transmission friction materials, friction disks and bands was begun in the 1940s.

The cohort was defined to include any man who had been employed at the plant for at least 1 month before 1959, omitting all that had worked at a nearby asbestos textile plant that closed in 1939. This cohort consisted of 3,515 men, of whom 36% had died by the end of follow-up (December 31, 1977). Follow-up of each worker was only begun past 20 years from first employment.

Information on dust levels from impinger measurements were available for the years 1930, 1935, 1936, and 1939. There was little other exposure information available until the 1970s. An industrial hygienist used these measurements and information on processes and jobs, environmental conditions and dust controls to estimate exposures by process and by period in units of mppcf. No conversion from mppcf to f/ml value was suggested by the authors, a conversion factor or between 1.4 and 10 is suggested by other studies. The most common value seems to be around 3 f/ml per mppcf, which has been observed in diverse environments such as mining and textile manufacture. This value was provisionally applied to this cohort, although this conversion has considerable uncertainty associated with it.

Total deaths and deaths from most individual causes investigated were elevated; these elevations were due primarily to increased deaths in the group working for <1 year. This pattern holds for lung cancer in particular; the SMR for lung cancer was highest (180) for persons exposed for <1 year. A similar pattern holds when the analysis was carried out by cumulative exposure (Table A-6); the SMR in the lowest exposure category is higher than in any other category. The linear relative risk lung cancer model provided a poor fit ($p=0.01$) to these data when the Connecticut rates were assumed to be appropriate for this cohort (fixing the parameter $\alpha=1$); use of U.S. rates gave similar results. However, the fit was adequate ($p=0.28$) if the background response is allowed to rise above that of Connecticut men (allowing the parameter α to vary). Although the reason for this increased response in persons that worked for a short period or have low exposures is not clear, the analysis in which the background response is allowed to vary appears to be the most appropriate. This analysis yields an estimate of $K_L=0.0$ $(\text{f-y/ml})^{-1}$, 90% CI: (0, 0.0017). The analysis with $\alpha=1$ yielded $K_L=0.0019$ $(\text{f-y/ml})^{-1}$, 90% CI: (0, 0.0061).

McDonald et al. did not find any mesotheliomas in this cohort. It is useful to determine the range of mesothelioma risk that is consistent with this negative finding. Although McDonald et al. do not furnish data in the form needed for this calculation, these data can be approximated from Table 1 of McDonald et al. (1984). In this table they list 511 deaths occurring after age 65. Assuming that the overall SMR of 108.5 held for persons over 65 years of age, the expected number of deaths is 511/1.085 = 471. The death rate in U.S. white males between 65 and 75 years of age is approximately 0.050 per year (from 1971 vital statistics). Therefore the number of person years observed in persons post 65 years of age is estimated as 471/0.050=9,420.

A lower bound on the person-years of follow-up between ages 45 and 65 can be estimated by assuming that follow-up was complete for this age group. First we estimate the number of persons that would have had to have been in the cohort to experience the observed deaths. Assuming that x persons in the cohort are alive at age 45, we have the following estimates of the number entering each successive five-year age interval and the corresponding number of deaths (based on death rates in 1,971 white males).

Age	Number Entering Interval	Number of Deaths in Interval	Person-Years in Interval
45-50	x	0.032x	4.9x
50-55	$x(1-0.00638)^5=0.97x$	0.052x	4.7x
55-60	$0.97x(1-0.01072)^5=0.92x$	0.076x	4.4x
60-65	$0.92x(1-0.01718)^5=0.84x$	0.11x	3.9x
65+	$0.84x(1-0.02681)^5=0.73x$		
TOTALS		0.27x	18.0x

Since there were 616 deaths in men between the ages of 45 and 65, the expected number of deaths is estimated as 616/1.085=567.7 expected deaths between ages of 45 and 60, the number of persons entering this age interval is estimated as x=567.7/0.27=2,100. The person-years is then estimated as (2,100)(17.964)=38,000.

Using the average age of beginning work of 30.95 years (McDonald et al. [1984], Table 3) yields the data in Table A-7. Moreover, the average duration of exposure in this cohort was 8.04 years and the average exposure level was 1.84 mppcf (McDonald et al. [1984], Table 3), which is equivalent to 1.84x3=5.52 fibers/ml. These data yields an estimate of K_M=0.0 and a 90% upper bound of $K_M=1.2\times10^{-9}$.

The best estimate of K_M was assumed to be zero. For uncertainty factors, F1 is assigned a value of 2.0 for reasons similar to those described for Quebec. F2 is assigned a value of 3.0 for this study because there is no conversion factor reported by the authors so that an average value of 3 for the range of conversion factors observed among the available studies (U.S. EPA 1986) was selected for use with this study. To derive an exposure-response factor for mesothelioma from this study, an upper bound had to be estimated by reconstructing the data because the authors do not provide the data in a form suitable for performing the required calculation. Therefore, F4M is assigned a value of 3 for this study. Thus:

F1 = 2.0
F2 = 3.0
F3 = 1.0
F4L = 1.0
F4M = 3.0

These values, when coupled with the statistical confidence limits, resulted in the uncertainty ranges for K_L and K_M shown in Table A-1 and A-2, respectively.

New Orleans Asbestos-Cement Plants. Hughes et al. (1987) report on follow-up through 1981 of a cohort of Louisiana workers from two asbestos cement plants studied previously by Weill et al. (1979). Although chrysotile, amosite and crocidolite were used at these plants, a group of workers at one of the plants were only exposed to chrysotile. The cohort contained 6,931 workers, of whom 95% were traced, compared to a 75% success in tracing by Weill et al. (1979). This improved trace was the result both of greater access to Social Security Administration records and greater availability of computerized secondary information sources (Dr. Hughes, personal communication).

Both of the plants have operated since the 1920s. Chrysotile was used predominantly in both plants. Some amosite was used in Plant 1 from the early 1940s until the late 1960s, constituting about 1% of some products, and crocidolite was used occasionally for approximately 10 years beginning in 1962. Plant 2 utilized only chrysotile, except that pipe production, which began in 1946 and was housed in a separate building, produced a final product that contained about 3% crocidolite. Since the total percentage of asbestos fiber in most asbestos cement products ranges from 15 to 28%, it is estimated that crocidolite constituted between 10 and 20% of the asbestos used to make cement pipe (Ontario Royal Commission 1984). Workers from Plant 2 that did not work in pipe production were exposed only to chrysotile.

Estimates of airborne dust levels were made for each job by month and year from midget impinger measurements initiated in the early 1950s. Levels estimated from initial samples in the 1950s were also assumed to hold for all earlier periods because no major dust control measures had been introduced prior to that time. New exposure data from Plant 2 became become available after the earlier study (Weill et al. 1979) was completed, and these, along with a complete review of all the exposure data, were used to revise the previous estimates of exposure. In Plant 1 the earlier and revised estimates were reasonably similar, but in Plant 2, the revised estimates tended to be about one-third of the previous estimates through the 1940s and about one-half the previous estimates thereafter. Based on 102 side-by-side measurements by midget impinger and PCM in various areas of one of the plants, Hammond et al. (1979) estimated an overall conversion factor of 1.4 fibers/ml per mppcf. There were substantial variations in this factor among different areas of the plant.

The principal cohort studied consisted of all workers who, according to company records, were employed for at least one month prior to 1970, had a valid Social Security number, and were first employed in 1942 or later (Plant 1), or in 1937 or later (Plant 2). Mortality experience was compared with that expected based on Louisiana rates.

Hughes et al. found no significant difference between the exposure responses for lung cancer in Plant 2 among workers exposed to chrysotile only and those who were also exposed to crocidolite in pipe production. A single lung cancer exposure response model adequately describes the lung cancer data from Plants 1 and 2 combined ($p \geq 0.42$, Table A-8). The fit of this model is good when Louisiana men are assumed to be an appropriate control group (fixing the parameter $\alpha=1$). This fit provides an estimate of $K_L=0.0040$ (fiber-y/ml)$^{-1}$, 90% CI: (0.0015, 0.0070). With α allowed to vary, the estimate is 0.0025 (fiber-y/ml)$^{-1}$, 90% CI: (0, 0.0066).

Six mesotheliomas were identified in the primary cohort studied by Hughes et al., two in Plant 1 and four in Plant 2. Four other mesotheliomas are known to have occurred, one among those initially employed in Plant 2 before 1937 and three among Plant 2 workers shortly after follow-up ended in 1981. A case control analysis conducted among Plant 2 workers found a relationship between mesothelioma risk and length of employment and proportion of time spent in the pipe area after controlling for length of exposure, which is consistent with a greater risk of mesothelioma from crocidolite exposure.

Data were not presented in the paper in the form required for estimating K_M. However, Hughes and Weill (1986) present estimates of mesotheliomas potency from several data sets, including the cohort studied in Hughes et al. and containing six mesotheliomas, but using a model slightly different from the 1986 EPA model (3). Estimating K_M by multiplying the potency estimated by the Hughes and Weill (1986) model by the ratio of the potency values estimated for another study using the 1986 U.S. EPA model and the Hughes-Weill (1986) model yielded the following estimates of K_M for the Hughes et al. (1987) data: 0.25×10^{-8} (Selikoff et al. 1979); 0.21×10^{-8} (Dement et al. 1983b); 0.27×10^{-8}(Seidman et al. 1979); and 0.43×10^{-8} (Finkelstein 1983). Based on these calculations, $K_M=0.30 \times 10^{-8}$ seems to be a reasonable estimate for the Hughes et al. cohort.

It would be worthwhile to estimate mesothelioma risk using additional follow-up that included the three cases that occurred shortly after follow-up ended. However, such an estimate should be no larger than about $K_M=0.45 \times 10^{-8}$. This is because, since there were six mesotheliomas in the cohort studied by Hughes et al., even if the additional person years of follow-up post-1981 is not taken into account, the three additional mesotheliomas would increase the estimate of K_M by only about 50%.

The finding by Hughes et al. (1987) of an association with crocidolite exposure implies that a smaller K_M would correspond to the chrysotile-only exposed group in Plant 2. Although Hughes et al. didn't furnish the data needed for precise estimation of K_M from this cohort, it is possible to make some reasonable approximations to this K_M. Since none of the six mesotheliomas occurred among workers exposed only to chrysotile, $K_M=0$ would be the point estimate derived from the data used by Hughes et al.

However, one mesothelioma was discovered in a person whose employment began in 1927 and thus was not eligible for inclusion in the cohort. This person was employed continuously for 43 years in the shingle production area, where only chrysotile was used. In an attempt to compute an alternative K_M using this one case, it was noted that the duration of observation of the Hughes et al. cohort was roughly equivalent to that of the Dement et al. (1983b) cohort. If the person-years from this cohort, categorized by years since first exposure, are adjusted by the ratio of the

sizes of Dement et al. and the Hughes et al. non-crocidolite-exposed cohort from Plant 2, one mesothelioma is assumed to occur (in 30+ years from first exposure category) and the average duration of exposure (2.5 years) and fiber level (11.2 fibers/ml) appropriate for the Hughes et al. cohort are applied to these data, a K_M=$0.2x10^{-8}$ is obtained.

The best estimate of K_M was assumed to be $0.2x10^{-8}$ for workers exposed only to chrysotile and $0.3x10^{-8}$ for workers exposed to both chrysotile and amphibole. For uncertainty factors, F1 is assigned a value of 2.0 for reasons similar to those described for Quebec. F2 is assigned a value of 1.5 because most early measurements were collected by midget impinger and the authors report using a conversion factor of 1.4 derived from paired measurements. Due to the lack of adequate data for estimating both the overall mesothelioma rate and a confidence interval for such rates and the consequent need to reconstruct the data (incorporating numerous assumptions) to be able to obtain the needed estimates, a value of 5.0 was assigned to the factor F4M for chrysotile exposures and 2.5 for mixed exposures. Thus:

F1 = 2.0
F2 = 1.5
F3 = 1.0
F4L = 1.0
F4M = 5.0

These values, when coupled with the statistical confidence limits, resulted in the uncertainty ranges for K_L and K_M shown in Tables A-1 and A-2.

South Carolina Textile Factory. Dement and coworkers (Dement et al. 1994; Dement and Brown 1998) conducted a retrospective cohort study of employees of a chrysotile textile plant in South Carolina. In an earlier study of this plant (Dement et al. 1982, 1983a,b), the cohort was defined as all white male workers who worked for one or more months between 1940 and 1965, and follow-up was through 1975. Dement et al. (1994) expanded the cohort to include black male and white female workers who met the entrance requirements, and extended follow-up through 1990, an additional 15 years. This expanded cohort included 1,247 white males (2.8% lost to follow-up), 1,229 white females (22.8% lost to follow-up) and 546 black males (7.8% lost to follow-up). A total of 1,259 deaths were identified, and a death certificate was located for all but 79 (6.2%) of the deaths.

Based on data from 5,952 air samples taken at the plant between 1930 and 1975, linear statistical models were used to reconstruct exposure levels, while taking into account textile processes, dust control methods, and job assignments (Dement et al. 1983a). For each worker, time spent in each job was multiplied by the estimated exposure level for that job to estimate cumulative exposure (f/ml-days). Based on regression analyses applied to 120 side-by-side particle and fiber counts, Dement (1980) estimated a f/ml to mppcf ratio of 2.9, 95% CI: (2.4, 3.5). Also, between 1968 and 1971 both impinger and PCM samples were collected (a total of 986 samples). Based upon a regression analysis of these data, Dement (1980) determined that a common conversion factor could be used for jobs except fiber preparation. For fiber preparation, a conversion factor of 7.8 was found, 95% CI: (4.7–9.1). For all other operations, a value of 2.5, 95% CI: (2.1–3.0) was calculated. Based on this information, Dement et al. (1983a) concluded

that a conversion factor of 3 was appropriate for all operations except preparation, for which a factor of 8 was adopted.

The underlying data for this cohort were obtained from the National Institute for Safety and Health (NIOSH). These data consisted of a work history file and a file with exposure levels by job category and time period. The work history file contained codes for race, sex, month and year of birth, vital status, month and year of death, and the department, operation, start date, and stop date for each job worked. The exposure level file contained the exposure start and stop dates and the exposure level (fiber/ml) by the plant code, the department code, and the operation code.

The cohort was defined as the white and black males and the white females who met the employment requirements described above. This cohort included 1,244 white males (1.5% lost to follow-up), 550 black males (7.5% lost to follow-up), and 1,228 white females (22.1% lost to follow-up).

Table A-9 shows observed and expected deaths for lung cancer among white males, black males and white females, categorized by cumulative exposure. This table shows an excess of lung cancers that exhibited an exposure response relationship. U.S. rates were used for calculating expected deaths, whereas South Carolina lung cancer rates are higher for white men, but slightly lower for white women and black men. Whereas twelve categories of cumulative exposure were used for fitting the model, these were been combined into seven categories for display in Table A-9. The model with $\alpha=1$ and α variable fit the data well ($p \geq 0.8$), and the hypothesis that $\alpha=1$ cannot be rejected ($p=0.19$). The estimate of K_L with $\alpha=1$ was 0.028 $(\text{f-y/ml})^{-1}$, 90% CI: (0.021, 0.037), and the estimate with α variable was $K_L=0.021$ $(\text{f-y/ml})^{-1}$, 90% CI: (0.012, 0.034). An analysis applied to white men alone gave somewhat higher estimates ($K_L=0.040$ $(\text{f-y/ml})^{-1}$ with $\alpha=1$, and $K_L=0.026$ $(\text{f-y/ml})^{-1}$ with α variable).

Two deaths were certified as due to mesothelioma on the death certificates. In addition, Dement et al. (1994) considered four other deaths as likely due to mesothelioma. The availability of the raw data from this study made it possible calculate K_M from this study using an "exact" likelihood approach based on Equation A-3 that did not involve any grouping of data, or use of average values. Using the six confirmed and suspected mesotheliomas, $K_M = 0.43 \times 10^{-8}$, 90% CI: $(0.20 \times 10^{-8}, 0.79 \times 10^{-8})$. Using the two confirmed mesotheliomas, $K_M = 0.14 \times 10^{-8}$, 90% CI: $(0.034 \times 10^{-8}, 0.38 \times 10^{-8})$.

For comparison purposes, K_M were also calculated using grouped data and applying Equation A-4, since this is the method that must be used with most studies. The data were divided into 10 categories by the tabulated values of Equation A-4. The K_M estimate based on the "exact" analysis was 2% greater than that based upon grouped data.

The best estimate of K_M was assumed to be the geometric mean of the MLE estimates computed using either confirmed or both confirmed and suspected mesotheliomas (0.25×10^{-8}). The statistical lower bound used for this estimate was the one based on confirmed cases and the upper bound used was the one based on confirmed and suspected cases.

Regarding uncertainty factors, F1 is assigned a value of 1.5 for this study to give credit for the reasonably complete sampling coverage of exposures by a combination of midget impinger and extensive PCM, and the formal statistical evaluation conducted to derive job-specific exposure estimates. However, the exposure estimates are still based on analyses of area rather than personal samples. Because multiple factors were used to convert midget impinger measurements to PCM based on side-by-side samples collected from specific areas (associated with specific operations) within the plant, a value of 1.0 is assigned for F2 for this study. The treatment of statistical confidence limits described above was considered adequate to account for the uncertainty in the number of mesotheliomas, and a value of K_M=1 was assigned. In summary:

F1 = 1.5
F2 = 1.0
F3 = 1.0
F4L = 1.0
F4M = 1.0

These uncertainty factors, when coupled with the statistical confidence limits, resulted in the uncertainty ranges for K_L and K_M shown in Tables A-1 and A-2.

McDonald et al. (1983a) conducted a cohort mortality study in the same South Carolina textile plant that was studied by Dement et al. (1994). Their cohort consisted of all men employed for at least 1 month before 1959 and for whom a valid social security record existed. This cohort consisted of 2,410 men, of whom 36% had died by the end of follow-up (December 31, 1977). Follow-up of each worker was begun past 20 years from first employment.

McDonald et al. (1983a) had available the same exposure measurements as Dement et al. (1983b) and used these to estimate cumulative exposures for each man in mppcf-y. In their review of the environmental measurements in which both dust and fiber concentrations were assessed, they found a particle to fiber conversion range of from 1.3 to 10.0 with an average of about 6 fibers/ml per mppcf. This value, which is intermediate between the values of 3 and 8 found by Dement et al. (1983b) for different areas of the same plant, will be used in the calculations involving the McDonald et al. (1983a) study.

McDonald et al. describe two practices at the plant that entailed very high exposures and which were not reflected in either their's or Dement and coworkers estimates: cleaning of burlap bags used in the air filtration system by beating them with buggy whips during the years 1937–1953, and the mixing of fibers, which was carried out between 1945 and 1964 by men with pitch forks and no dust suppression equipment.

A strong exposure response for lung cancer was observed (Table A-10), which parallels the results of Dement et al. (1994). Unlike Dement et al., McDonald et al. used South Carolina men as the control group rather than U.S. men. Use of this control group provided an adequate description of the data and lung cancer potency values estimated both with α=1 and allowing α to vary provided excellent descriptions of the data ($p \geq 0.88$) and the hypothesis α=1 could not be rejected (p=0.80). Assuming α=1 resulted in K_L=0.012 $(f\text{-}y/ml)^{-1}$, 90% CI: (0.0075, 0.016), and when α was allowed to vary, K_L=0.010 $(f\text{-}y/ml)^{-1}$, 90% CI: (0.0044, 0.025). These results are

reasonably consistent with the potency estimated from Dement et al. (1994), and the differences can be largely accounted for by the different assumptions regarding the fiber/particle ratio.

McDonald et al. (1983a) found one case of mesothelioma in this cohort, apparently the same one discovered by Dement et al. (1983b): a man born in 1904 who died in 1967 and worked at the plant for over 30 years. Since this study was conducted exactly as McDonald et al. (1984), the same method used there to reconstruct person-years by years from first exposure can be applied to this cohort as well. The reconstructed data are listed in Table A-11. The estimated potency MLE is K_M=0.088 x10^{-8}, with a 90% CI: (0.0093x10^{-8}, 0.32x10^{-8}).

For uncertainty factors, F1 is assigned a value of 2.0 for reasons similar to those described for Quebec. F2 is assigned a value of 1.0 because McDonald essentially used the same data that Dement and coworkers used to estimate conversion factors (see above), although they favored a slightly higher mean value. We used the values favored by Dement when evaluating this study.

Unlike the study by Dement and coworkers (for which we received the raw data so that we could calculate the exposure-response factor and the attendant confidence interval for mesothelioma directly), the mesothelioma data published in the McDonald study of this facility was not suitable to estimating confidence bounds. Thus the data had to be reconstructed, which required incorporation of numerous assumptions. To account for the uncertainty associated with the reconstruction, F4M is assigned a value of 3 for this study. Thus:

F1 = 2.0
F2 = 1.0
F3 = 1.0
F4L = 1.0
F4M = 3.0

These uncertainty factors, when coupled with the statistical confidence limits, resulted in the uncertainty ranges for K_L and K_M shown in Tables A-1 and A-2.

Predominant Crocidolite Exposure

Wittenoom, Australia Mine and Mill. de Klerk et al. (1994) followed a cohort of 6,904 men and women employed at a crocidolite mine and mill in Wittenoom, Australia. This cohort was followed through 1999 and the raw data were obtained through the courtesy of Dr. de Klerk. The data consisted of a record number, date of birth, sex, employment start date, total days of employment, average exposure level (f/ml), cumulative exposure (f-year/ml), date of last contact, ICD code for cause of death, indicator variable for mesothelioma death, and date of death if applicable.

A number of subjects from the full cohort were removed from the analysis reported herein: 412 because the sex was not designated as male; one because the date of last contact was missing; 1,275 subjects because the follow-up period was <5 years; 41 because the number of days worked was 0 or missing. After these subjects were removed, the cohort consisted of 5,173 men who were employed at Wittenoom Gorge between 1943 and 1966.

The concentrations of fibers greater than 5 μm in length as measured by PCM were measured at various work sites in a survey conducted in 1966. Job category data were obtained from employment records and supplemented by records from the Perth Chest Clinic and the Western Australian Mineworkers Relief Fund. The concentration measurements and job category information were used to estimate the exposure level for each subject in the cohort (de Klerk et al. 1994). The exposure levels were high with a median of 17.8 (fiber/ml). The durations of employment were low with a median of 128 days.

There were 251 lung cancer deaths in the cohort. Table A-12 shows the observed, expected, and predicted lung cancer deaths among the males categorized by cumulative exposure (fiber-year/ml). The number of expected lung cancer deaths are based on Australian lung cancer mortality rates. With no allowance for difference between the background lung cancer death rates among Australia and the members of this cohort (α=1), the fit of the model is poor ($p<0.01$). Allowing for difference in the background lung cancer death rates (a variable), the model provides a reasonably good fit to the data ($p=0.10$) and estimates K_L=0.0047 (fiber-year/ml)$^{-1}$, 90% CI: (0.0017, 0.0087). The hypothesis α=1 can be rejected with high confidence ($p<0.01$).

There were 165 mesotheliomas in the cohort. The availability of the raw data from this study made it possible calculate K_M from this study using an "exact" likelihood approach based on Equation A-3 that did not involve any grouping of data, or use of average values. With this approach, $K_M=7.95\times10^{-8}$, 90% CI: (6.97×10^{-8}, 9.01×10^{-8}).

For comparison purposes, K_M were also calculated using grouped data and applying Equation A-4, since this is the method that must be used with most studies. The K_M estimate based on the "exact" analysis was 12% lower than the estimate based upon grouped data.

Regarding uncertainty factors, F1 is assigned a value 2.0 for this study for reasons similar to those described for Quebec. F2 is assigned a value of 1.0 because measurements were conducted using PCM so that conversion is unnecessary for this study. All other factors are also assigned a value of 1.0 because there are no other unique limitations. Thus:

F1 = 2.0
F2 = 1.0
F3 = 1.0
F4L = 1.0
F4M = 1.0

These uncertainty factors described earlier, when coupled with the statistical confidence limits, resulted in the uncertainty ranges for K_L and K_M and shown in Table A-1 and A-2.

Predominant Amosite Exposure

Patterson, N.J. Insulation Factory. Seidman et al. (1986) studied a cohort of 820 men (mostly white) who worked at an amosite asbestos factory that operated in Patterson, New Jersey from 1941 through 1954. The men began work between 1941 and 1945 and follow-up was through 1982. The follow-up of a worker began 5 years following the beginning of employment.

Workers who had prior asbestos exposure were not included in the cohort, and follow-up was stopped when a worker was known to have begun asbestos work elsewhere (6 men). Exposures were generally brief, as 76% were exposed for ≤2 years, although a few were exposed for as long as 10 years.

No asbestos exposure measurements are available for this plant. Estimates of exposures in particular jobs were made based on air measurements made between 1967 and 1970 at plants in Tyler, Texas and Port Allegheny, Pennsylvania that were operated by the same company and made the same products using some of the same machinery as the Patterson facility. The estimated median exposure level was 50 f/ml. Amosite was the only type of asbestos used at the plant.

Seidman et al. cross-categorized lung cancer deaths by cumulative exposure (eight categories of f-y/ml) and length of time worked (seven categories, Seidman et al. 1986, Table XXXIV). Although this table apparently was created by categorizing workers by their final cumulative exposure (rather than categorizing person-years of follow-up by the cumulative exposure to that point in time, which is more appropriate for calculating a K_L), because exposures were brief this likely made little difference. Expected number of lung cancer deaths were based on age- and year-specific rates for New Jersey white males.

Table A-13 shows the results of applying the lung cancer model to these data, after collapsing the table by summing over length-of-time worked. Results were highly dependent upon whether or not the background lung cancer mortality rate was assumed to be equal to that predicted by the comparison population of New Jersey white males (equivalent to $\alpha=1$). The test for departure from the null hypothesis, $\alpha=1$, was highly significant, and the maximum likelihood estimate was $\alpha=3.3$. Similarly, the model gave a poor overall fit to the data with $\alpha=1$ ($p<0.01$), but the fit was quite good when α was allowed to vary ($p=0.90$). The estimated potency parameter, K_L, also was highly dependent upon the assumption regarding the parameter, α. The estimate of K_L was 0.062 $(\text{f-y/ml})^{-1}$, 90% CI: (0.050, 0.076), when α was fixed at $\alpha=1$, and 0.011 $(\text{f-y/ml})^{-1}$, 90% CI: (0.0058, 0.019), when α was allowed to vary, a 6-fold difference. The lung cancer model was also fit to the data cross-classified by both cumulative exposure and length of time worked, allowing α to assume a different value in each category of time worked. Although the estimated values of α tended to increase with increasing duration of exposure, allowing different values of α did not significantly improve the fit ($p=0.64$).

The reason for this behavior is not clear. There is no indication that workers with shorter durations experienced disproportionately high mortality, since, as noted above, α tended to increase with increasing duration of exposure. Although it is possible that cumulative exposure is not the appropriate exposure metric, it is difficult to envision what metric would predict this response, so long as a linear model is assumed. It is also possible that a linear model for relative risk is not correct and a supralinear model is more appropriate, or that the increased risk is not proportional to the background risk, as assumed by this simple relative risk model. Finally, it is possible that the background rate in this population is significantly greater than that in the comparison population, although it seems unlikely that it could be 3 times greater as suggested by the model.

Seidman et al. (1986) discovered 17 deaths from mesothelioma in this population. Table III of Seidman et al. categorized mesothelioma deaths and person-years of observation by years since onset of work. In order to apply the 1986 U.S. EPA mesothelioma model it is necessary to have estimates of the duration of exposure and level of exposure for each category. Using the categorization of the members of the cohort by duration of work in Table XXIII of Seidman et al., it was estimated that the mean duration of work was 1.5 years. Using data from Seidman et al. Table XIV, an average cumulative exposure was for each category of time from onset of exposure by weighting exposures according to the expected total number of deaths. These averages were divided by 1.5 years to obtain the average fiber concentrations in Table A-14. The estimated exposure levels decrease with time since onset, which is consistent with higher mortality among more heavily exposed workers.

The 1986 mesothelioma model provided an adequate fit to these data (p=0.35), although it over-predicted somewhat the number of cases in the highest latency category (>35 years). The estimate of K_M was 3.9×10^{-8}, 90% CI: (2.6×10^{-8}, 5.7×10^{-8}).

Regarding uncertainty factors, F1 is assigned a value of 3.5 for this study because exposure concentrations were not measured at this facility at all. Rather exposures were estimated (as described in Lemon et al. [1980]) based on measurements collected at another facility in Tyler, Texas (see below) that manufactured the same products from the same source of raw materials using some of the same equipment, which was moved from the Patterson plant to the plant in Tyler. Because the measurements collected in Tyler were analyzed by PCM, no conversion factor is required. Thus, F2 is assigned a value of 1.0 for this study. All other factors are also assigned a factor of 1.0 due to lack of other remarkable limitations. Thus:

F1 = 3.5
F2 = 1.0
F3 = 1.0
F4L = 1.0
F4M = 1.0

These uncertainty factors, when coupled with the statistical confidence limits, resulted in the uncertainty ranges for K_L and K_M shown in Table A-1 and A-2.

Tyler, Texas Insulation Factory. Levin et al. (1998) studied the mortality experience of 1,121 men who formerly worked at a plant in Tyler, Texas that manufactured asbestos pipe insulation. The plant operated from 1954 through February 1972. The plant used the same raw materials and some of the same equipment that was used in the Patterson, New Jersey plant that was studied by Seidman et al. (1986). The asbestos used was amosite from the Transvaal region of South Africa. The insulation was manufactured from a mixture that contained 90% amosite asbestos.

Environmental surveys were conducted at the plant in 1967, 1970, and 1971, with average fiber concentrations ranging from 15.9 through 91.4 f/ml. An average exposure of 45 f/ml is assumed for this plant, which is near the middle of this range obtained in the three surveys. It is also consistent with average levels assumed for the Patterson, New Jersey plant, which operated under very similar conditions.

The cohort consisted of 744 whites, 305 non-white (mostly black), and 72 with missing race (assumed to be white, based on hiring practices at that time). For the entire cohort, the median age of first employment was 25 years, and the mean duration of employment was 12.7 months (range of one day to 17.3 years). Follow-up was through 1993. Death certificates were obtained for 304 of the 315 men known to be dead. In the mortality analysis only white men were evaluated and follow-up started 10 years after first employment. After additional exclusions of men with missing birth dates or missing employment information, the cohort analyzed in the mortality analysis consisted of 753 former workers, among whom 222 deaths were recorded. These deaths were compared with those expected based on age, race and sex-specific U.S. rates.

There was an excess of deaths from respiratory cancer (SMR=277, based on 36 deaths, not including four deaths from mesothelioma). Table A-15 contains observed and expected numbers of deaths from respiratory cancer, categorized by duration of exposure. Cumulative exposure in f-y/ml was estimated by multiplying the duration of exposure times the assumed average fiber level of 45 f/ml. There was an excess of lung cancer deaths in the lowest exposure group (23 observed, 8.9 expected), and consequently the model with $\alpha=1$ did not fit these data ($p<0.01$), and the hypothesis $\alpha=1$ could be rejected ($p<0.01$). The K_L with α variable was $K_L=0.0013$, 90% CI: (0, 0.0060). With $\alpha=1$, $K_L=0.013$ $(\text{f-y/ml})^{-1}$, 90% CI: (0.0055, 0.022).

Four mesotheliomas were reported in this study. However, the data are not presented in a form that would permit application of the U.S. EPA 1986 mesothelioma model.

Regarding uncertainty factors, F1 is assigned a value of 3.0 for this study because, although exposure concentrations were measured at this facility, the data are sparse so that only an overall average concentration for the entire plant could be derived. Because the measurements collected were analyzed by PCM, no conversion factor is required. Thus, F2 is assigned a value of 1.0 for this study. All other factors are also assigned a factor of 1.0 due to lack of other remarkable limitations. Thus:

F1 = 3.0
F2 = 1.0
F3 = 1.0
F4L = 1.0

These uncertainty factors, when coupled with the statistical confidence limits, resulted in the uncertainty range for K_L shown in Table A-1.

Predominant Tremolite-Actinolite Exposure

Libby, Montana Vermiculite Mine. Amandus and Wheeler (1987) conducted a retrospective cohort study of 575 men who were exposed to tremolite-actinolite while working at a vermiculite mine and mill in Libby, Montana. A dry mill began operation in 1935 and a wet mill began operating in the same building as the dry mill in 1950 (Amandus et al. 1987).

A total of 376 impinger samples were available that had been collected during 1950–1969, although only 40 of these were collected prior to 1965. In addition 4,118 PCM samples were available from the period 1967–1982. Exposure estimates for years later than 1968 were based

on historical measures of fiber concentrations (f/ml), and those for earlier years were based on concentrations measured by midget impinger (mppcf) and converted to f/ml assuming a conversion ratio of 4 f/ml per mppcf. This conversion factor was derived from 336 impinger samples collected during 1965–1969 and 81 filter samples collected during 1967–1971. Individual cumulative fiber exposure estimates (f-y/ml) were computed from job-specific exposure estimates and work histories (Amandus et al. 1987).

The cohort consisted of all men hired prior to 1970 and employed for at least 1 year in either the mine or the mill. Follow-up was through December 31, 1981. The vital statuses of 569 of the men (99%) were determined and death certificates were obtained for 159 of the 161 who were deceased.

Smoking information was available for 161 men employed between 1975 and 1982 and with at least 5 years of tenure. The proportion of these workers who smoked (current or former) was 84% compared to 67% among U.S. white males during the same time period.

A total of 20 deaths from lung cancer were observed (9 expected, SMR=223.2, using U.S. white males as the comparison population). Table A-16 (based on Amandus and Wheeler 1987, Table II) shows that the excess occurred mainly in workers whose cumulative exposure exceeded 400 f-y/ml (10 observed, 1.7 expected). The 1986 U.S. EPA lung cancer model fit these data adequately ($p \geq 0.25$) both with $\alpha=1$ and α variable, and the hypothesis $\alpha=1$ could not be rejected ($p=0.8$). With $\alpha=1$, K_L was estimated as 0.0061 $(\text{f-y/ml})^{-1}$, 90% CI: (0.0029, 0.010), and with α variable, K_L= 0.0051 $(\text{f-y/ml})^{-1}$, 90% CI: (0.0011, 0.020).

Amandus and Wheeler (1987) observed 2 deaths from mesothelioma in this cohort. However, information on these cases was not sufficient to permit application of the 1986 U.S. EPA mesothelioma model.

For uncertainty factors, F1 is assigned a value of 2.0 for reasons similar to those described for Quebec. F2 is assigned a value of 1.5 because most early measurements were collected by midget impinger and the authors report using a conversion factor of 4 derived from temporally overlapping (but not paired) measurements. All other uncertainty factors were assigned a value of 1.0. Thus:

F1 = 2.0
F2 = 1.5
F3 = 1.0
F4L = 1.0

These uncertainty factors, when coupled with the statistical confidence limits, resulted in the uncertainty range for K_L shown in Table A-1.

McDonald et al. (1986) also conducted a cohort study of workers at the Libby, Montana vermiculite mine and mill. Their cohort was composed of 406 workers employed prior to 1963 for at least 1 year. Follow-up was until July 1983. Vital status was determined for all but one man and death certificates were obtained for 163 of the 165 men who had died. Cumulative exposures (f-y/ml) were estimated for each worker using work histories based on 42 job

categories, and 1,363 environmental measurements, including samples analyzed by PCM (f/ml) and by midget impinger (mppcf).

A total of 23 deaths from lung cancer were observed (SMR=303, based on Montana rates). Table A-17 shows these deaths categorized by cumulative exposure (based on Table 4 of McDonald et al. 1986). Both the models with $\alpha=1$ and α variable fit these data adequately ($p \geq 0.16$) although the test of $\alpha=1$ was marginally significant ($p=0.11$). The estimate of K_L with $\alpha=1$ was 0.011, $(\text{f-y/ml})^{-1}$, 90% CI: (0.0055, 0.017), and with α variable, $K_L = 0.0039$ $(\text{f-y/ml})^{-1}$, 90% CI: (0.00067, 0.012).

McDonald et al. (1986) observed 2 deaths from mesothelioma. However, information on these cases was not sufficient to permit application of the 1986 U.S. EPA mesothelioma model.

Because this study and the Amandus study used virtually the same data and very similar approaches to analysis, the same values are assigned to uncertainty factors for this study that are assigned for the Amandus and Wheeler study. These factors, when coupled with the statistical confidence limits, resulted in the uncertainty range for K_L shown in Table A-1.

Exposure to Mixed Fiber Types

British Friction Products Factory. Berry and Newhouse (1983) conducted a mortality study of 13,460 workers in a factory in Britain that manufactured brake blocks, brake and clutch linings, and other friction materials. Only chrysotile was used at the plant except for two relatively short periods before 1945 when crocidolite was used in the production of railway blocks.

The cohort studied consisted of all men or women employed at the plant between 1941 and 1977. Follow-up was to the end of 1979 and the mortality experience was examined after 10 years from first exposure. Airborne dust measurements were only available from 1967 onward and these were made using the PCM method. Fiber concentrations in earlier years were estimated by reproducing earlier working conditions using knowledge of when processes were changed and exhaust ventilation introduced.

Deaths from all causes were less than expected both prior to 10 years from first employment (185 observed versus 195.7 expected) and afterward (432 observed versus 450.8 expected). There was no indication of an effect of employment at the plant upon lung cancer; there were 51 lung cancers >10 years from first employment compared to 47.4 expected. A significant deficit of gastrointestinal cancers was observed after 10 years from first employment (25 observed versus 35.8 expected, $p=0.04$).

A linear exposure response model relating cumulative exposure and lung cancer was fit to case-control data presented by Berry and Newhouse. The resulting K_L was 0.00058 $(\text{f-y/ml})^{-1}$ and the 95% upper limit was 0.0080 $(\text{f-y/ml})^{-1}$. This estimate was used as the best estimate of K_L, and the lower confidence bound was assumed to be zero.

A case control study on mesothelioma deaths showed that 8 of the 11 cases had been exposed to crocidolite and another possibly had intermittent exposure to crocidolite. The other two had been employed mostly outside the factory and possibly had other occupational exposures to

asbestos. The case control analysis showed that the distribution of cases and controls in respect to exposure to crocidolite was quite unlikely assuming no association with crocidolite. This indicates that some, and possibly all, of the eight mesotheliomas with crocidolite exposure were related to this exposure. The data were not presented in a form that permitted a quantitative estimate of mesothelioma risk.

Regarding uncertainty factors, F1 is assigned a value of 2.0 for this study because, although the manner in which unmeasured exposure was estimated in this study is different than for that reported for the majority of other studies (see, for example, Quebec), it is unlikely to introduce greater uncertainty. Rather than extrapolating measured estimates to earlier times based on expert judgements, judgements were used to simulate earlier conditions at the plant and exposures were measured directly. Because the measurements collected were analyzed by PCM, no conversion factor is required. Thus, F2 is assigned a value of 1.0 for this study. An uncertainty factor F4L=1.5 was included to account for the fact that α was not estimated. F3 was assigned a factor of 1.0 due to lack of other remarkable limitations. Thus:

F1 = 2.0
F2 = 1.0
F3 = 1.0
F4L = 1.5

These factors, when coupled with the statistical confidence limits, resulted in the uncertainty range for K_L shown in Table A-1.

Ontario Asbestos-Cement Plant. Finkelstein (1984) studied mortality among a group of 535 exposed and 205 unexposed employees of an Ontario asbestos-cement factory who had been hired before 1960 and who had been employed for at least 1 year. This cohort contained the cohort studied by Finkelstein (1983) and which required at least 9 years of employment for membership. Follow-up continued until 1977 or 1981.

The plant produced asbestos cement pipe from 1948, asbestos cement board from 1955–1970, and manufacture of asbestos insulation materials was added in 1960. Both chrysotile and crocidolite were used in each batch processed in the pipe process, but only chrysotile was used in the cement board operation. Crocidolite constituted approximately 20% of the asbestos used in the pipe process (Ontario Royal Commission 1984).

Fiber concentrations in various work areas and for various epochs were estimated from membrane filter samples taken after 1969, impinger measurements taken during 1949, 1954, 1956, 1957, and semiannually during the 1960s, and information on changes in dust control methods. Finkelstein judged that the resulting exposure estimates were "probably accurate to within a factor of three or five." Exposures of maintenance workers were not estimated, and the exposure response analysis consequently involved only the unexposed workers (N=205) and the production workers (N=428).

Only 21 deaths from lung cancer were observed among production workers. Based on these deaths, Finkelstein compared age-standardized lung cancer mortality rates in production workers after a 20-year latency, categorized into five groups according to their cumulative exposure

through 18 years from date of first employment (Finkelstein 1984, Table 7). Mortality rates were standardized with respect to age and latency using the man-years distribution in the cohort as a whole as the standard. Using similarly standardized mortality rates in Ontario males as the comparison population, lung cancer rates were elevated in all five categories, and Finkelstein found a significant exposure-response trend. However, the trend was not monotone, as rates increased up to the middle exposure category and decreased thereafter (Table A-18).

These data may be put into a form roughly equivalent to the more conventional age-adjusted comparison of observed and expected lung cancer deaths by dividing the rates in the exposed group by that of Ontario men. (The rate for unexposed workers was not used because it was based on only 3 deaths.) The results of this are shown in Table A-18, which also shows the results of fitting the 1986 U.S. EPA lung cancer model both assuming the Ontario rates were appropriate for this cohort (fixing the parameter α=1) and not making this assumption (allowing the parameter α to vary). Neither approach provided an adequate fit to these data ($p \leq 0.05$) and the test of α=1 was marginally significant (p=0.07). The maximum likelihood estimate of α was 4.26, which seems too large to be due to differences in smoking habits. The K_L estimate with α=1 was 0.048 $[\text{f-y/ml}]^{-1}$, 90% CI: (0.028, 0.074). With α allowed to vary the estimate was K_L=0.0029 $[\text{f-y/ml}]^{-1}$, 90% CI: (0, 0.037). The fact that the lower limit was zero indicates that the exposure-response trend was not significant when the background was allowed to vary.

Based on a "best evidence" classification of cause of death, Finkelstein identified 17 deaths from mesothelioma among production workers. Table 3 of Finkelstein (1984) gives these mesotheliomas categorized by years since first exposure. This table also provides the mortality rate, from which can be calculated the person-years of observation. Finkelstein states that the average cumulative exposure for production workers was about 60 f-y/ml, but does not provide information for determining duration and level of exposure separately. CHAP (1983) used an average exposure of 9 f/ml for a subcohort of production workers, although they provided no support for this assumption. If this value is assumed to be appropriate for the expanded cohort, the average duration is estimated as about 60/9=6.7 years. However these values are uncertain. Table A-19 presents the result of applying the 1986 U.S. EPA mesothelioma model to the Finkelstein (1984) data based on these assumptions. The mesothelioma model describes these data adequately (p=0.26) and provides an estimate of $K_M = 18 \times 10^{-8}$, 90% CI: (13×10^{-8}, 24×10^{-8}).

Regarding uncertainty, F1 is assigned a value of 4 because Finkelstein indicates that exposure estimates derived for this study are probably good to within a factor of 3 or 4. Findlestein also notes that many of the assumptions employed to extrapolate exposures were only weakly supported by limited, earlier impinger measurements. The source of the conversion factor employed to link impinger measurements and PCM measurements in this study is unclear. Therefore a value of 3.0 is assigned to F2. Because data for evaluating mesothelioma incidence was not provided in a format suitable for deriving confidence intervals, so that some reconstruction was required, a value of 2.0 is assigned for F4M. All other factors are also assigned a factor of 1.0 due to lack of other remarkable limitations. Thus:

F1 = 4.0
F2 = 3.0
F3 = 1.0
F4L = 1.0
F4M = 2.0

These factors, when coupled with the statistical confidence limits, resulted in the uncertainty ranges for K_L and K_M shown in Tables A-1 and A-2.

Swedish Asbestos-Cement Plant. Albin et al. (1990) studied workers at a Swedish plant that operated from 1907 to 1978 and produced various asbestos cement products, including sheets, shingles, and ventilation pipes. The asbestos handled was mainly chrysotile (>95%). Crocidolite was used before 1966, but never exceeded 3–4% of the total asbestos. Amosite was used for a few years in the 1950s but never exceeded 18% of the total asbestos used. Fiber length classes were the commercial grades 3–7, and all asbestos was milled prior to incorporation into products.

Impinger and gravimetric dust measurements were available for 1956–1969, and PCM measurements after 1969. These data, along with information on production and dust control, were used to estimate exposures for different jobs and periods of time.

The cohort contained 2,898 men and was defined as all male employees who worked for at least 3 months between 1907 and 1977. A reference cohort was composed of 1,233 men who worked in other industries in the region and who were not known to have worked with asbestos. Vital status of both groups was determined through 1986. Follow-up of both began after 20 years from first employment.

Excluding mesothelioma, other respiratory cancers were not significantly increased. Albin et al. present relative risks of these respiratory cancers and corresponding 95% CIs for three categories of cumulative exposure (Table A-20), based on Poisson regression with control for age and calendar year. In order to obtain crude estimates of the range of K_L that are consistent with these data, the 1986 U.S. EPA lung cancer relative risk model was fit, assuming that the Ln (RR) were normally distributed with fixed variances computed from the reported confidence intervals for the RR. Although elevated, the RR did not exhibit an exposure response, and the hypothesis $\alpha=1$ was not rejected ($p=0.13$). In this analysis K_L was not significantly different from zero, regardless of whether α was fixed at 1.0 or estimated. With $\alpha=1$ the estimate of K_L was 0.019 $(\text{f-y/ml})^{-1}$, 90% CI: (0, 0.065), and $K_L=0.00067$ $(\text{f-y/ml})^{-1}$, 90% CI: (0, 0.036) with α estimated.

Thirteen mesotheliomas were identified among exposed workers and one in the referent population, and a significant exposure response was observed with increasing cumulative exposure. Unfortunately, the mesothelioma data were not presented in a format that would permit application of the 1986 U.S. EPA mesothelioma model.

Regarding uncertainty, F1 is assigned a value of 4 due to the sparsity of data and the need to extrapolate. Several assumptions were incorporated into the extrapolations performed that were

based, among other things, on the scarcity of raw-material asbestos during World War II. All other factors are also assigned a factor of 1.0 due to lack of other remarkable limitations. Thus:

F1 = 4.0
F2 = 1.0
F3 = 1.0
F4L = 1.0

These factors, when coupled with the statistical confidence limits, resulted in the uncertainty range for K_L shown in Table A-1.

Belgium Asbestos-Cement Plant. Lacquet et al. (1980) conducted a roentgenologic, asbestosis, and mortality study in a Belgium asbestos cement factory employing about 2,400 employees that annually processed about 39,000 tons of asbestos, of which 90% was chrysotile, 8% crocidolite, and 2% amosite. The mortality study considered male workers who worked in the factory for at least 12 months during the 15-year period 1963–1977. Apparently no minimal latency was required before follow-up began.

Fiber counts were available for the years 1970–1976; fiber levels were estimated for as far back as 1928, but these estimates were considered to be "only good guesses at best." Individual exposures were estimated in fiber-years from work histories and estimated yearly concentrations in four work areas.

The incidence of respiratory cancer was very close to that which was expected in a Belgium population of matched age and sex (Table A-21). The models with α=1 (p=0.51) and α variable (p=0.39) gave similar results and the hypothesis α=1 was not rejected (p=0.77). With α=1, the estimate of K_L was 0.0 $(\text{f-y/ml})^{-1}$, 90% CI: (0, 0.0010). With α estimated, $K_L=6.8\text{x}10^{-5}$ $(\text{f-y/ml})^{-1}$, 90% CI: (0, 0.0021).

One death was due to pleural mesothelioma. Unfortunately, the data were not presented in a way that allowed the estimation of K_M.

Regarding uncertainty, F1 is assigned a value of 4 due to the sparsity of data and the need to extrapolate. Much of the data appear to be based on PCM, so that conversion is not necessary. All other factors are also assigned a factor of 1.0 due to lack of other remarkable limitations. Thus:

F1 = 4.0
F2 = 1.0
F3 = 1.0
F4L = 1.0

These factors, when coupled with the statistical confidence limits, resulted in the uncertainty range for K_L shown in Table A-1.

Retirees from U.S. Asbestos Products Company. Enterline et al. (1986) extended follow-up through 1980 for a cohort of U.S. retirees from a large asbestos products company that had been the subject of an earlier report (Henderson and Enterline 1979). Products manufactured by the company included textiles, cement shingles, sheets, insulation and cement pipe. Exposure was predominately to chrysotile in most operations, although amosite predominated in insulation production, and crocidolite in manufacture of cement pipe. Each worker's exposure was estimated from dust measurements in mppcf obtained from environmental surveys that started in the mid-1950's and were extrapolated back in time by the company industrial hygienist. No data are provided for conversion from mppcf to PCM in f/ml. Given the wide range of products manufactured, this conversion likely varied according to operation. Conversions calculated in different environments have ranged from 1.4 to 10, the most common value being around 3 f/ml per mppcf, which has been observed in diverse environments such as mining and textile manufacture. This value was provisionally applied to this cohort.

The cohort consisted of 1,074 white males who retired from the company during 1941–1967, and who were exposed to asbestos in production or maintenance jobs. The average duration of employment was 25 years. Follow-up started at age 65 or at retirement if work continued past age 65. By the end of follow-up in 1980, 88% were deceased.

Overall, respiratory cancer was significantly increased (SMR=258 in comparison to U.S. rates, based on 79 observed deaths). Enterline et al. (1986) categorized lung cancer deaths by cumulative exposure (their Table 4). Results of applying the 1986 U.S. EPA lung cancer model to these data are shown in Table A-22. Although both the model with $\alpha=1$ and α variable fit the data adequately ($p \geq 0.75$), the test of $\alpha=1$ was not rejected ($p=0.24$). With $\alpha=1$ the estimate of K_L was 0.0021 $(\text{f-y/ml})^{-1}$, 90% CI: (0.0015, 0.0027). With α variable, $K_L=0.0011$ $(\text{f-y/ml})^{-1}$, 90% CI: (0.00041, 0.0028).

From the death certificates Enterline et al. identified eight deaths from mesothelioma. These data were not presented in a form that permitted application of the 1986 U.S. EPA mesothelioma model.

Regarding uncertainty, F1 is assigned a value of 2.0 for this study for reasons similar to those described for Quebec. Because the manner employed for deriving the conversion factor used to convert impinger counts to fiber concentrations is not documented, a value of 3.0 is assigned to F2 for this study. All other factors are also assigned a factor of 1.0 due to lack of other remarkable limitations. Thus:

F1 = 2.0
F2 = 3.0
F3 = 1.0
F4L = 1.0

These factors, when coupled with the statistical confidence limits, resulted in the uncertainty range for K_L shown in Table A-1.

U.S. Insulation Applicators. Selikoff and Seidman (1991) reported on follow-up through 1986 of a cohort of 17,800 asbestos insulation applicators that had been followed through 1976 by Selikoff et al. (1979). The cohort consisted of men enrolled as members of the insulator's union in the United States and Canada. Deaths were classified both based on the information the death certificate, and using "best evidence," in which death certificate information was augmented by clinical data, histopathological material and X-rays.

Based on the composition of insulation material, it seems likely that these workers were exposed to substantial amounts of chrysotile and amosite. Data on insulator's exposures were reviewed by Nicholson (1976), who concluded that average exposures of insulation workers in past years could have ranged 10–15 f/ml and could have been 15–20 f/ml in marine construction. U.S. EPA (1986) assumed a value of 15 f/ml as an overall average, with an associated 3-fold uncertainty. This estimate of 15 f/ml will be used provisionally here as well.

The form of the data provided in Selikoff and Seidman (1991) is not particularly suitable for calculating K_L. Table 4 of Selikoff and Seidman (1991) contain observed and expected deaths from lung cancer (determined from either death certificates or best information) categorized by years from first exposure (<15, 15–19, 20–24, ..., 50+). Death certificate information was utilized herein to facilitate comparisons with expected deaths (based on the mortality experience of U.S. white males), which were also based on death certificates. Lung cancer was significantly increased over expected, except for the category of <15 years from onset of exposure. Selikoff and Seidman did not provide information on the duration of exposure. The U.S. EPA (1986, page 90) assumed an average exposure duration of 25 years. Assuming that all workers worked exactly 25 years and were exposed to 15 f/ml, the data in Table 4 of Selikoff and Seidman can be used to categorize lung cancer deaths by cumulative exposure lagged 10 years. The result is shown in Table A-23. The 1986 U.S. EPA lung cancer model provided a reasonable fit to these data with α variable ($p=0.12$), but not with $\alpha=1$ ($p<0.01$). Also, the hypothesis that $\alpha=1$ could be rejected ($p<0.01$). The estimate of K_L with α variable was 0.0018 $(\text{f-y/ml})^{-1}$, 90% CI: (0.00065, 0.0038). With $\alpha=1$, $K_L=0.0087$ $(\text{f-y/ml})^{-1}$, 90% CI: (0.0081, 0.0093).

Based on best evidence, Selikoff and Seidman (1991) found 458 mesotheliomas in this cohort. Table A-24 shows these deaths categorized by years from onset (based on Selikoff and Seidman 1991, Tables 5 and 6). Table A-24 also shows the results of fitting the 1986 U.S. EPA mesothelioma model to these data, assuming, as above, that workers worked for 25 years and were exposed to 15 f/ml. The 1986 U.S. EPA mesothelioma model provided a poor fit to these data ($p<0.01$), as it overestimates by more than a factor of 2 the number of mesothelioma deaths after 50+ years from first exposure. The estimate of K_M was $1.3\text{x}10^{-8}$, 90% CI: ($1.2\text{x}10^{-8}$, $1.4\text{x}10^{-8}$).

Regarding uncertainty, F1 is assigned a value of 4.0 for this study because data employed to estimate exposure is not facility-specific, but represents general, industry-wide exposure estimates derived from limited data. F3 is assigned a value of 2 for this study because the study provides no information on worker histories. F4L is assigned a value of 2 for this study because the data presented in the study were not provided in a form suitable for fitting the lung cancer model. Thus, the data had to be partially reconstructed. Other factors are also assigned a factor of 1.0 due to lack of other remarkable limitations. Thus:

F1 = 4.0
F2 = 1.0
F3 = 2.0
F4L = 2.0
F4M = 1.0

These factors, when coupled with the statistical confidence limits, resulted in the uncertainty ranges for K_L and K_M shown in Tables A-1 and A-2.

Pennsylvania Textile Plant. McDonald et al. (1983b) report on mortality in an asbestos plant located near Lancaster, Pennsylvania that produced mainly textiles, but also some friction materials. About 3,000 to 6,000 tons of chrysotile were processed annually at the plant, which began operation in the early 1900s. Crocidolite and amosite were used from 1924 onward; about 3–5 tons of raw crocidolite were processed annually and the use of amosite reached a peak of 600 tons during World War II.

The cohort consisted of all men employed for at least 1 month prior to 1959 and who had a valid record with the Social Security Administration. This group consisted of 4,022 men, of whom 35% had died by the end of follow-up (December 31, 1977). Follow-up of each worker was only begun past 20 years from first employment.

To estimate exposures, McDonald et al. had available reports of surveys conducted by the Metropolitan Life Insurance Company during the period 1930–1939, Public Health Service surveys conducted during 1967 and 1970, and company measurements made routinely from 1956 onward. These data were used to estimate by department and year in units of mppcf.

The lung cancer mortality in this cohort exhibited a significant exposure response trend (Table A-25), which was partially due to a deficit of cancers in the group exposed to <10 mppcf-y (21 with 31.4 expected). A survey of those employed in the plant in 1978 revealed a larger per cent of nonsmokers (25%) than were found in the other plants studied by these researchers (McDonald et al. 1983a, 1984), although this finding was based on a sample of only 36 workers. Regardless of the reason for this shortfall in the number of lung cancers, it appears that the most appropriate analysis is that in which the background is allowed to vary; this analysis fits the data well ($p>0.7$), whereas the analysis which assumes the Pennsylvania rates are appropriate provides a marginal fit ($p=0.08$). The hypothesis $\alpha=1$ was rejected ($p=0.01$). Consequently, the former analysis is judged to be the most appropriate (allowing the parameter α to vary). McDonald et al. (1983b) did not provide a factor for converting from mppcf to f/ml. Assuming that 3 f/ml is equivalent to one mppcf, the resulting estimate of lung cancer potency with α variable was 0.018 $(\text{f-y/ml})^{-1}$, 90% CI: (0.0075, 0.045). With $\alpha=1$, $K_L=0.0057$ $(\text{f-y/ml})^{-1}$, 90% CI: (0.0027, 0.0094).

A diagnosis of mesothelioma was specified on 14 death certificates (ten pleural and four peritoneal). Thirty other deaths were given the ICD code 199 (malignant neoplasms of other and unspecified sites) and the diagnosis given in many of these cases was said to be consistent with an unrecognized mesothelioma. McDonald et al. (1983b) Table 3 lists the average age at beginning of employment as 28.92 and the average duration of employment as 9.18 years, and their Table 1 lists 191, 667, and 534 deaths as occurring before age 45, between 45 and 65, and

after 65 years of age, respectively. Assuming that ½ of the deaths given the ICD code 199 might have been due to mesotheliomas, the total number of mesotheliomas in this cohort is estimated to be 23. Proceeding as in the mesothelioma analysis carried out for the McDonald et al. (1984) data, the data in Table A-26 were generated. Noting that the age since first exposure categories in which the mesotheliomas occurred is irrelevant as far as estimating K_M is concerned, the estimate of K_M is 1.1×10^{-8}, 90% CI: (0.76×10^{-8}, 1.5×10^{-8}). These estimates are uncertain due to the uncertainty regarding the number of mesotheliomas in the cohort.

Regarding uncertainty, F1 is assigned a value of 2.0 for this study for reasons similar to those described for Quebec. Because the manner employed for deriving the conversion factor used to convert impinger counts to fiber concentrations is not documented, a value of 3.0 is assigned to F2 for this study. A factor of 2.0 is assigned for F4M because the number of mesotheliomas observed in this study are reported to be estimates expected to be good to within a factor of 2. Thus:

F1 = 2.0
F2 = 3.0
F3 = 1.0
F4L = 1.0
F4M = 2.0

These factors, when coupled with the statistical confidence limits, resulted in the uncertainty ranges for K_L and K_M shown in Tables A-1 and A-2.

Rochdale, England Textile Factory. Peto et al. (1985) studied a textile factory in Rochdale, England that has been the subject of a number of earlier reports (Peto et al. 1977; Peto 1980a,b). Peto et al. (1985) has the most complete follow-up (through 1983) and emphasizes assessment of risk. The factory, which began working with asbestos in 1879, used principally chrysotile, but approximately 5% crocidolite was used between 1932 and 1968.

Quantitative estimates of risk were based on a subgroup of Peto et al. (1985) "principal cohort" consisting of all men first employed in 1933 or later who had worked in scheduled areas or on maintenance and had completed 5 years of service by the end of 1974. In the analyses of interest relating to lung cancer, follow-up only begins 20 years after the beginning of employment and exposure during the last 5 years of follow-up is not counted.

Routine sampling using a thermal precipitator began at 23 fixed sampling points in 1951. Comparisons of particle counts and fiber counts taken in 1960 and 1961 were used to convert between particles/ml and f/ml. Dust levels prior to 1951 were assumed to be the same as those observed during 1951–1955 for departments for which no major changes had been made. In departments in which conditions had improved, higher levels were assigned. These levels and work histories were used to assign individual exposure estimates. A conversion factor of 34 particles/ml per f/ml was determined by comparing average results obtained by the Casella thermal precipitator (particles/ml) with Ottway long running thermal precipitator (f/ml) at the same sampling point during 1960 and 1961. However, a conversion factor of 35.3 was used by Peto et al. (1985) for the sake of consistency with earlier work, and this factor will be used here as well.

After 20 years from first employment, there were 93 lung cancer deaths with only 64.6 expected. Using a lung cancer model essentially the same as the 1986 U.S. EPA model, Peto et al. estimated K_L=0.0054 (f-y/ml)$^{-1}$ for the entire cohort, and K_L=0.015 (f-y/ml)$^{-1}$ when the analysis was restricted to men first employed in 1951 or later. Peto et al. felt that the most plausible explanation for this difference was that it was largely due to chance and also possibly to the chance that exposure to the most carcinogenic fibers was not reduced as much as changes in particle counts from 1951 to 1960 would suggest.

Table A-27 displays the exposure response data based on men first employed in 1933 or later for lung cancer based on shows that the excess occurred mainly in workers whose cumulative exposure exceeded 400 f-y/ml (10 observed, 1.7 expected). The 1986 U.S. EPA lung cancer model fit these data adequately ($p \geq 0.63$) both with α=1 and α variable, and the hypothesis α=1 could not be rejected (p=0.57). With α=1, K_L was estimated as 0.0052 (f-y/ml)$^{-1}$, 90% CI: (0.0028, 0.0079), and with α variable, K_L=0.0041 (f-y/ml)$^{-1}$, 90% CI: (0.0012, 0.0087).

Ten mesotheliomas were observed in the cohort used by Peto et al. for quantitative analysis (an 11th case who was exposed for 4 months and died 4 years later was omitted because the short latency made it unlikely that this case was related to exposure at the factory). Observed mesotheliomas and corresponding person-years of observation by duration of service and years since first employment (Peto et al. 1985, Table 8) are shown in Table A-28. An overall average exposure was estimated by applying the Peto mesothelioma model to the data in Table A-28 with a single exposure estimate selecting the value that gave the smallest least squares fit of this model to the mesothelioma data. The fitting was carried out both unweighted and by weighting by the person years, with resulting estimates of 360 and 322 particles/ml, respectively; the latter value was the one selected. Using the conversion factor of 35.3 particles/ml per f/ml, the estimated average exposure is 322/35.2=9.1 f/ml. The 1986 U.S. EPA mesothelioma model fit these data well, and the resulting estimate of mesothelioma potency (Table A-28) was K_M=1.3x10^{-8}, 90% CI: (0.74x10-8, 2.1x10^{-8}).

Regarding uncertainty, F1 is assigned a value of 2.0 for this study for reasons similar to those described for Quebec. Because a conversion factor was derived for measurements collected using Otway long-running thermal precipitators and PCM measurements based on measurements of each collected under similar conditions (but not side-by-side), a value of 2 is assigned to F2. Thus:

F1 = 2.0
F2 = 2.0
F3 = 1.0
F4L = 1.0
F4M = 1.0

These factors, when coupled with the statistical confidence limits, resulted in the uncertainty ranges for K_L and K_M shown in Tables A-1 and A-2.

REFERENCES

Albin M; Jakobsson K; Attewell R; Johansson L; Welinder H. Mortality and Cancer Morbidity in Cohorts of Asbestos Cement Workers and Referents. *British Journal of Industrial Medicine.* 79(9):602–610. September. 1990.

Amandus HE; Wheeler R. The Morbidity and Mortality of Vermiculite Miners and Millers Exposed to Tremolite-Actinolite: Part II. Mortality. *American Journal of Industrial Medicine* 11:15–26. 1987.

Amandus HE; Wheeler R; Jankovic J; Tucker J. The Morbidity and Mortality of Vermiculite Miners and Millers Exposed to Tremolite-Actinolite: Part I. Exposure Estimates. *American Journal of Industrial Medicine.* 11:1–14. 1987.

Armstrong BK; de Klerk NH; Musk AW; Hobbs MST. Mortality in Miners and Millers of Crocidolite in Western Australia. *British Journal of Industrial Medicine.* 45:5–13. 1988.

Berry G; Newhouse ML. Mortality of Workers Manufacturing Friction Materials Using Asbestos. *British Journal of Industrial Medicine.* 40:1–7. 1983.

CHAP (Chronic Hazard Advisory Panel on Asbestos). Report to the U.S. Consumer Product Safety Commission. July. 1983.

Cox D; Oakes DV. *Analysis of Survival Data.* Cox DR; Hinkley DV (eds.). Chapman and Hall, London. 1984.

de Klerk NH; Musk AW; Armstrong BK; Hobbs MST. Diseases in Miners and Millers of Crocidolite from Wittenoom, Western Australia: A Further Follow-up to December 1986. *Annals of Occupational Hygiene.* 38(Suppl 1):647–655. 1994.

Dement JM. Estimation of Dose and Evaluation of Dose-Response in a Retrospective Cohort Mortality Study of Chrysotile Asbestos Textile Workers. Ph.D. Thesis. The University of North Carolina at Chapel Hill. 1980.

Dement JM; Brown DP. Cohort Mortality and Case-Control Studies of White Male Chrysotile Asbestos Textile Workers. *Journal of Clean Technology, Environmental Toxicology, and Occupational Medicine.* 7:1052–1062. 1998.

Dement JM; Harris RL; Symons MJ; Shy CM. Estimates of Dose-Response for Respiratory Cancer Among Chrysotile Asbestos Textile Workers. *Annals Occupational Hygiene.* 26(1-4):869–887. 1982.

Dement JM; Harris RL; Symons MJ; Shy CM. Exposures and Mortality Among Chrysotile Workers. Part I: Exposure Estimates. *American Journal of Industrial Medicine.* 4:399–419. 1983a.

Dement JM; Harris RL; Symons MJ; Shy CM. Exposures and Mortality Among Chrysotile Workers. Part II: Mortality. *American Journal of Industrial Medicine*. 4:421–433. 1983b.

Dement JM; Brown DP; Okun A. Follow-up Study of Chrysotile Asbestos Textile Workers: Cohort Mortality and Case-Control Analysis. *American Journal of Industrial Medicine*. 26:431–447. 1994.

Enterline PE; Harley J; Henderson V. Asbestos and Cancer -- A Cohort Followed to Death. Graduate School of Public Health, University of Pittsburgh. 1986.

Finkelstein MM. Mortality Among Long-Term Employees of an Ontario Asbestos-Cement Factory. *British Journal of Industrial Medicine*. 40:138–144. 1983.

Finkelstein MM. Mortality Among Employees of an Ontario Asbestos-Cement Factory. *American Review of Respiratory Disease*. 129:754-761. 1984.

Hammond EC; Selikoff IJ; Seidman H. Asbestos Exposure, Cigarette Smoking and Death Rates. *Annals New York Academy of Sciences*. 330:473–490. 1979.

Henderson VL; Enterline PE. Asbestos Exposure: Factors Associated with Excess Cancer and Respiratory Disease Mortality. *Annals New York Academy of Sciences*. 330:117–126. 1979.

Hughes JM; Weill H. Asbestos Exposure: Quantitative Assessment of Risk. *American Review of Respiratory Disease*. 133:5–13. 1986.

Hughes JM; Weill H; Hammad YY. Mortality of Workers Employed at Two Asbestos Cement Plants. *British Journal of Industrial Medicine*. 44:161-174. 1987.

Lacquet LM; VanderLinden L; Lepoutre J. Roentgenographic Lung Changes, Asbestosis and Mortality in a Belgian Asbestos-Cement Factory. In *Biological Effects of Mineral Fibres*, Wagner JC (ed.). IARC Sci Publ. pp. 783–793. 1980.

Lemon RA; Dement JM; Wagoner JK. Epidemiology of asbestos-related diseases. *Environmental Health Perspective*. 34:1-11. 1980.

Levin JL; McLarty JW; Hurst GA; Smith AN; Frank AL. Tyler Asbestos Workers: Mortality Experience in a Cohort Exposed to Amosite. *Occupational and Environmental Medicine*. 55:155–160. 1998.

Liddell FDK. Unpublished raw mesothelioma data provided to Dr. Wayne Berman by Dr. FDK Liddell from multiple studies of the 1891–1920 Birth Cohort of Quebec Chrysotile Miners and Millers most recently described in Liddell et al. 1997. 2001.

Liddell FDK; McDonald AD; McDonald JC. The 1891–1920 Birth Cohort of Quebec Chrysotile Miners and Millers: Development From 1904 and Mortality to 1992. *Annals of Occupational Hygiene*. 41:13–36. 1997.

McDonald JC; Liddell FDK; Gibbs GW; Eyssen GE; McDonald AD. Dust Exposure and Mortality in Chrysotile Mining, 1910–1975. *British Journal of Industrial Medicine*. 37:11–24. 1980a.

McDonald JC; Gibbs GW; Liddell FDK. Chrysotile Fibre Concentration and Lung Cancer Mortality: A Preliminary Report. In *Biological Effects of Mineral Fibres*. Wagner JC (ed). IARC Scientific Publications. pp. 811–817. 1980b.

McDonald AD; Fry JS; Wooley AJ; McDonald JC. Dust Exposure and Mortality in an American Chrysotile Textile Plant. *British Journal of Industrial Medicine*. 39:361–367. 1983a.

McDonald AD; Fry JS; Woolley AJ; McDonald JC. Dust Exposure and Mortality in an American Factory Using Chrysotile, Amosite, and Crocidolite in Mainly Textile Manufacture. *British Journal of Industrial Medicine*. 40:368–374. 1983b.

McDonald AD; Fry JS; Woolley AJ; McDonald JC. Dust Exposure and Mortality in an American Chrysotile Asbestos Friction Products Plant. *British Journal of Industrial Medicine*. 41:151–157. 1984.

McDonald JC; McDonald AD; Armstrong B; Sebastien P. Cohort Study of Mortality of Vermiculite Miners Exposed to Tremolite. *British Journal of Industrial Medicine*. 43:436–444. 1986.

McDonald JC; Liddell FDK; Dufresne A; McDonald AD. The 1891–1920 Birth Cohort of Quebec Chrysotile Miners and Millers: Mortality 1976–1988. *British Journal of Industrial Medicine*. 50:1073–1081. 1993.

Nicholson WJ. Part III. Recent Approaches to the Control of Carcinogenic Exposures. Case Study 1: Asbestos - The TLV Approach. *Annals New York Academy of Science*. 271:152–169. 1976.

Nicholson WJ; Selikoff IJ; Seidman H; Lilis R; Formby P. Long-Term Mortality Experience of Chrysotile Miners and Millers in Thetford Mines, Quebec. *Annals New York Academy of Sciences*. 330:11–21. 1979.

Ontario Royal Commission. Report of the Royal Commission on Matters of Health and Safety Arising form the Use of Asbestos in Ontario. Volume 3. 1984.

Peto J. Lung Cancer Mortality in Relation to Measured Dust Levels in an Asbestos Textile Factory. In *Biological Effects of Mineral Fibres*. Wagner JC (ed.). IARC Scientific Publications. pp. 829–836. 1980a.

Peto J. The Incidence of Pleural Mesothelioma in Chrysotile Asbestos Textile Workers. In *Biological Effects of Mineral Fibres*. Wagner JC (ed.). IARC Scientific Publications. pp. 703–711. 1980b.

Peto J; Doll R; Howard SV; Kinlen LJ; Lewinsohn, HC. A Mortality Study Among Workers in an English Asbestos Factory. *British Journal of Industrial Medicine*. 34:169–173. 1977.

Peto J; Seidman H; Selikoff IJ. Mesothelioma Mortality in Asbestos Workers: Implications for Models of Carcinogenesis and Risk Assessment. *British Journal of Cancer*. 45:124–135. 1982.

Peto J; Doll R; Hermon C; Binns W; Clayton R; Goffe T. Relationship of Mortality to Measures of Environmental Asbestos Pollution in an Asbestos Textile Factory. *Annals of Occupational Hygiene*. 29(3):305–355. 1985.

Piolatto G; Negri E; LaVecchia C; Pira E; Decarli A; Peto J. An Update of Cancer Mortality Among Chrysotile Asbestos Miners in Balangero, Northern Italy. *British Journal of Industrial Medicine*. 47:810–814. 1990.

Rubino GF; Piolatto GW; Newhouse ML; Scansetti G; Aresini GA; Murray R. Mortality of Chrysotile Asbestos Workers at the Balangero Mine, Northern Italy. *British Journal of Industrial Medicine*. 36:187–194. 1979.

Seidman H. Short-Term Asbestos Work Exposure and Long-Term Observation -- July 1984 Update. Department of Epidemiology, American Cancer Society. 1984.

Seidman H; Selikoff IJ; Hammond EC. Short-Term Asbestos Work Exposure and Long-Term Observation. *Annals New York Academy of Sciences*. 330:61–89. 1979.

Seidman H; Selikoff IJ; Gelb SK. Mortality Experience of Amosite Asbestos Factory Workers: Dose-Response Relationships 5 to 40 Years After Onset of Short-Term Work Exposure. *American Journal of Industrial Medicine*. 10(5/6):479–514. 1986.

Selikoff IJ; Seidman H. Asbestos-Associated Deaths among Insulation Workers in the United States and Canada, 1967–1987. *Annals of the New York Academy of Sciences*. 643:1–14. 1991.

Selikoff IJ; Hammond EC; Seidman H. Mortality Experience of Insulation Workers in the United States and Canada 1943–1976. *Annals New York Academy of Sciences*. 330:91–116. 1979.

U.S. EPA (U.S. Environmental Protection Agency). Airborne Asbestos Health Assessment Update. Report 600/8-84-003F, U.S. Environmental Protection Agency. 1986.

Venzon D; Moolgavkar S. A Method for Computing Profile-likelihood-based Confidence Intervals. *Applied Statistics*. 37:87-94. 1988.

Weill H. 1994. Cancer Mortality in Chrysotile Mining and Milling: Exposure-Response. Asbestos-Cement. *Annals of Occupational Hygiene*. 38(4):412. 1994.

Weill H; Hughes J; Waggenspack C. Influence of Dose and Fibre Type on Respiratory Malignancy Risk in Asbestos Cement Manufacturing. *American Review of Respiratory Disease*. 120:345–354. 1979.

Table A-1. Lung Cancer Exposure-Response Coefficients (K_L) Derived from Various Epidemiological Studies

Fiber Type	Operation	Cohort	EPA (1986) K_L*100	Reference	This Update K_L*100	90% Confidence Interval	Uncertainty Interval[a]	Reference
Chrysotile	Mining and Milling	Quebec mines and mills	0.06	McDonald et al. 1980b	0.029	(0.019, 0.041)	(0.0085, 0.091)	Liddell et al. 1997
			0.17	Nicholson et al. 1979				
		Italian mine and mill	0.081	Piolatto et al. 1990	0.051	(0, 0.57)	(0, 1.1)	Piolatto et al. 1990
	Friction Products	Connecticut plant	0.01	McDonald et al. 1984	0	(0, 0.17)	(0, 0.62)	McDonald et al. 1984
	Cement Manufacture	New Orleans plants			0.25	(0, 0.66)	(0, 1.5)	Hughes et al. 1987
	Textiles	South Carolina plant	2.8	Dement et al. 1983b	2.1	(1.2, 3.4)	(0.81, 5.1)	Dement et al. 1994[b]
			2.5	McDonald et al. 1983a	1	(0.44, 2.5)	(0.22, 4.9)	McDonald 1983a
Crocidolile	Mining and Milling	Wittenoom			0.47	(0.17, 0.87)	(0.084, 1.7)	de Klerk et al. 1994[c]
Amosite	Insulation Manufacture	Patterson, NJ factory	4.3	Seidman 1984	1.1	(0.58, 1.9)	(0.17, 6.6)	Seidman et al. 1986
		Tyler, Texas factory			0.13	(0, 0.6)	(0, 1.8)	Levin et al. 1998
Tremolite	Vermiculite Mines and Mills	Libby, Montana			0.51	(0.11, 2.0)	(0.049, 4.4)	Amandus and Wheeler 1987
					0.39	(0.067, 1.2)	(0.03, 2.8)	McDonald et al. 1986
Mixed	Friction Products	British factory	0.058	Berry and Newhouse 1983	0.058	(0, 0.8)	(0, 1.8)	Berry and Newhouse 1983

Table A-1. Lung Cancer Exposure-Response Coefficients (K_L) Derived from Various Epidemiological Studies *(continued)*

Fiber Type	Operation	Cohort	EPA (1986) K_L*100	Reference	This Update K_L*100	90% Confidence Interval	Uncertainty Interval[a]	Reference
	Cement Manufacture	Ontario factory	4.8	Finkelstein 1983	0.29	(0, 3.7)	(0, 22)	Finkelstein 1984
		New Orleans plants	0.53	Weill 1979, 1994	0.25	(0, 0.66)	(0, 1.5)	Hughes et al. 1987
		Swedish plant			0.067	(0, 3.6)	(0, 14)	Albin et al. 1990
		Belgium factory			0.0068	(0, 0.21)	(0, 0.84)	Laquet et al. 1980
	Factory workers	US. retirees	0.49	Henderson and Enterline 1979	0.11	(0.041, 0.28)	(0.011, 1.0)	Enterline et al. 1986
	Insulation Application	U.S. insulation workers	0.75	Seilkoff et al. 1979	0.18	(0.065, 0.38)	(0.012, 2.1)	Seilkoff and Seidman 1991
	Textiles	Pennsylvania plant	1.4	McDonald et al. 1983b	1.8	(0.75, 4.5)	(0.2, 16)	McDonald et al. 1983b
		Rochedale plant	1.1	Peto 1980a	0.41	(0.12, 0.87)	(0.046, 2.3)	Peto et al. 1985

[a]Uncertainty Interval formed by combining 90% confidence interval with uncertainty factors in Table A-3.
[b]With supplemental raw data from Terri Schnorr (NIOSH) and Dement
[c]With supplemental unpublished raw data with follow-up through 2001

Table A-2. Mesothelimoa Exposure-Response Coefficients (K_M) Derived from Various Epidemiological Studies

Fiber Type	Operation	Cohort	EPA (1986) K_M*100	Reference	This Update K_M*100	90% Confidence Interval	Uncertainty Interval[a]	Reference
Chrysotile	Mining and Milling	Asbestos, Quebec			0.013	(0.0068, 0.022)	(0.003, 0.049)	Liddell et al. 1997[b]
		Thedford Mines			0.021	(0.014, 0.029)	(0.0065, 0.065)	Liddell et al. 1997[b]
	Friction Products	Connecticut plant			0	(0, 0.12)	(0, 0.65)	McDonald et al. 1984
	Cement Manufacture	New Orleans plant			0.2	–	(0.033, 1.2)	Hughes et al. 1987
	Textiles	South Carolina plant			0.25	(0.034, 0.79)	(0.023, 1.2)	Dement et al. 1994[c]
					0.088	(0.0093, 0.32)	(0.0025, 1.2)	McDonald et al. 1983a
Crocidolile	Mining and Milling	Wittenoom			7.9	(7, 9)	(3.5, 18)	de Klerk et al. 1994[d]
Amosite	Insulation Manufacture	Patterson, NJ factory	3.2	Seidman 1984	3.9	(2.6, 5.7)	(0.74, 20)	Seidman et al. 1986
Mixed	Cement Manufacture	Ontario factory	12	Finkelstein 1983	18	(13, 24)	(2, 160)	Finkelstein 1984
		New Orleans plant			0.3	–	(0.089, 1)	Hughes et al. 1987
	Factory Workers	Asbestos, Quebec			0.092	(0.04, 0.18)	(0.018, 0.39)	Liddell et al. 1997[b]
	Insulation Application	U.S. insulation workers	1.5	Seilkoff et al. 1979	1.3	(1.2, 1.4)	(0.25, 6.5)	Seilkoff and Seidman 1991
	Textiles	Pennsylvania plant			1.1	(0.76, 1.5)	(0.17, 6.6)	McDonald et al. 1983b
		Rochedale plant	1	Peto 1980; Peto et al. 1982	1.3	(0.74, 2.1)	(0.28, 5.6)	Peto et al. 1985

[a]Uncertainty Interval formed by combining 90% confidence interval with uncertainty factors in Table A-3.
[b]With supplemental raw data from Liddell
[c]With supplemental raw data from Terri Schnorr (NIOSH) with Dement
dWith supplemental unpublished raw data with follow-up through 2001

Table A-3. Uncertainty Factors Used to Develop Uncertainty Intervals for Exposure-Response Coefficients (K_L's and K_M's)

		Uncertainty Factors for Estimating Exposure			Special Uncertainty Factors		Combined Uncertainty		
Fiber Type Operation	Cohort	Uncertainty Estimating Exposure Concentrations F1	Uncertainty Converting to PCM F2	Uncertainty Assigning Job Histories F3	Uncertainty for Special Lung Cancer Limitations F4	Uncertainty for Special Mesothelioma Limitations F4M	Lung Cancer	Meso-thelioma	Reference
Chrysotile									
Mining and Milling	Quebec	2	1.5				2.2	2.2[a]	Liddell et al. 1997
	Asbestos, Quebec	2	1.5				NR	2.2[a]	Liddell et al. 1997
	Thedford Mines	2	1.5				NR	2.2[a]	Liddell et al. 1997
	Italian mine and mill	2					2.0	ND	Piolatto et al. 1990
Friction Products	Connecticut plant	2	3			3	3.7	5.5	McDonald et al. 1984
Cement Manufacture	New Orleans plant	2	1.5			5	2.2	6.0	Hughes et al. 1987
Textiles	South Carolina plant	1.5					1.5	1.5	Dement et al. 1994[b]
	South Carolina plant	2				3	2.0	3.7	McDonald et al. 1983a
Crocidolile									
Mining and Milling	Wittenoom	2					2.0	2.0	de Klerk et al. 1994[c]
Amosite									
Insulation Manufacture	Patterson, NJ factory	3.5					3.5	3.5	Seidman et al. 1986

Table A-3. Uncertainty Factors Used to Develop Uncertainty Intervals for Exposure-Response Coefficients (K_L's and K_M's) *(continued)*

Fiber Type Operation	Cohort	Uncertainty Factors for Estimating Exposure: Uncertainty Estimating Exposure Concentrations F1	Uncertainty Factors for Estimating Exposure: Uncertainty Converting to PCM F2	Uncertainty Factors for Estimating Exposure: Uncertainty Assigning Job Histories F3	Special Uncertainty Factors: Uncertainty for Special Lung Cancer Limitations F4	Special Uncertainty Factors: Uncertainty for Special Mesothelioma Limitations F4M	Combined Uncertainty: Lung Cancer	Combined Uncertainty: Meso-thelioma	Reference
	Tyler, Texas factory	3					3.0	ND	Levin et al. 1998
Tremolite									
Vermiculite Mines and Mills	Libby, Montana	2	1.5				2.2	ND	Amandus and Wheeler 1987
	Libby, Montana	2	1.5				2.2	ND	McDonald et al. 1986
Mixed									
Friction Products	British factory	2			1.5		2.2	ND	Berry and Newhouse 1983
Cement Manufacture	Ontario factory	4	3			2	5.9	6.7	Finkelstein 1984
	New Orleans plant	2	1.5			2.5	2.2	3.4	Hughes et al. 1987
	Swedish plant	4					4.0	ND	Albin et al. 1990
	Belgium factory	4					4.0	ND	Laquet et al. 1980
Factory Workers	U.S. retirees	2	3				3.7	ND	Enterline et al. 1986
	Asbestos, Quebec	2	1.5				NR	2.2a	Liddell et al. 1997
Insulation Application	U.S. insulation workers	4		2	2		5.5	4.7	Seilkoff and Seidman 1991

Table A-3. Uncertainty Factors Used to Develop Uncertainty Intervals for Exposure-Response Coefficients (K_L's and K_M's) *(continued)*

		Uncertainty Factors for Estimating Exposure			Special Uncertainty Factors		Combined Uncertainty		
Fiber Type Operation	Cohort	Uncertainty Estimating Exposure Concentrations F1	Uncertainty Converting to PCM F2	Uncertainty Assigning Job Histories F3	Uncertainty for Special Lung Cancer Limitations F4	Uncertainty for Special Mesothelioma Limitations F4M	Lung Cancer	Meso-thelioma	Reference
Textiles	Pennsylvania plant	2	3			2	3.7	4.4	McDonald et al. 1983b
	Rochedale plant	2	2				2.7	2.7	Peto et al. 1985

[a]With supplemental raw data from Liddell et al. 1997 for mesothelioma
[b]With supplemental raw data from Terri Schnorr (NIOSH) with Dement
[c]With supplemental unpublished raw data with follow-up through 2001

NOTES:
Values for uncertainty factors not listed in the table are assumed to be equal to one.
A description of the manner in which each of the values presented in this table was assigned is presented under the descriptions of individual studies in Appendix A.
NR means no raw data. These are the data sets from Quebec for which we had access only to raw data for mesothelioma. Thus, lung cancer rates could not be determined.
NR means not determined. These are the data sets for which mesothelioma data were either lacking or were unuseable.

Table A-4
Cancer of Lung, Trachea, or Bronchus by Cumulative Exposure Level among Workers in Quebec Chrysotile Mines and Mills
Liddell et al. (1997)

mpcf-yr		(f-yr)/ml	SMR	Expected	Observed	Predicted	
Range	Mean	Mean				$\alpha = 1$	$\alpha = 1.15$
[0, 3)	1.5	4.71	1.12	67.0	75	67.1	76.9
[3, 10)	6.5	20.41	1.27	50.4	64	50.8	58.2
[10, 30)	20	62.8	1.03	59.2	61	60.8	69.2
[30, 60)	45	141.3	1.32	45.5	60	48.1	54.3
[60, 100)	80	251.2	1.45	42.1	61	46.4	51.8
[100, 200)	150	471	1.27	52.8	67	63.0	68.8
[200, 300)	250	785	1.1	31.8	35	42.1	44.8
[300, 400)	350	1099	1.46	19.9	29	28.8	30.1
[400, 1000)	700	2198	1.84	47.8	88	91.1	89.9
>= 1000	1500	4710	2.97	15.8	47	46.5	43.0
Totals				432.2	587	544.7	587.0

		$\alpha = 1$ (fixed)	$\alpha = 1.15$ (MLE)
$K_L * 100$		0.041	0.029
(90% Confidence Interval)		(0.032, 0.051)	(0.019, 0.041)
Goodness of Fit	P-value	0.18	0.58
Test of H_0: $\alpha = 1$	P-value	0.014	

Table A-5
Lung Cancer Mortality among Chrysotile Asbestos Miners in Balangero, Northern Italy
Piolatto et al. (1990)

f-y/ml Range	Mean	Observed	Expected	Predicted α = 1	Predicted α = 0.937
< 100	50	4	5.1	5.2	4.9
[100, 400)	250	8	6.1	6.6	6.4
>= 400	600	10	8.7	10.5	10.7
Totals		22	19.9	22.3	22.0

		α = 1 (fixed)	α = 0.937 (MLE)
K_L * 100		0.035	0.051
(90% Confidence Interval)		(0, 0.15)	(0, 0.57)
Goodness of Fit	P-value	0.75	0.45
Test of H_0: α = 1	P-value	0.88	

Table A-6
Lung Cancer Mortality among Workers in a Chrysotile Asbestos Friction Products Plant in Connecticut
McDonald et al. (1984)

mpcf-yr Range	mpcf-yr Mean	(f-yr)/ml Mean	SMR	Expected	Observed	Predicted α = 1	Predicted α = 1.49
< 10	5	15	167.4	32.9	55	33.8	49.0
[10 , 20)	15	45	101.7	5.9	6	6.4	8.8
[20 , 40)	30	90	105.4	4.7	5	5.5	7.1
[40 , 80)	60	180	162.8	3.7	6	4.9	5.5
>=80	110	330	55.22	1.8	1	2.9	2.7
Totals				49.0	73	53.6	73.0

		α = 1 (fixed)	α = 1.49 (MLE)
K_L * 100		0.19	0
(90% Confidence Interval)		(0, 0.61)	(0, 0.17)
Goodness of Fit	P-value	0.01	0.28
Test of H_0: α = 1	P-value	0.001	

Table A-7
Mesothelioma Mortality among Connecticut Friction Product Plant Workers
McDonald et al. (1984)

Years After First Exposure Range	Mean	Duration of Exposure	f/ml	Person Years	Observed	Predicted
[14, 34)	22	8.04	5.52	37742	0	0.0
>= 34	39	8.04	5.52	9420	0	0.0
Totals				47162	0	0.0

$K_M * 10^8$	0
(90% Confidence Interval)	(0, 0.12)
Goodness of Fit P-Value	1.00

Table A-8
Lung Cancer Mortality among Workers Employed in Two Asbestos Cement Manufacturing Plants in New Orleans, Louisiana
Hughes et al. (1987)

mpcf-yr Range	mpcf-yr Mean	(f-yr)/ml Mean	Observed	Expected	Predicted α = 1	Predicted α = 1.14
Plant 1 Employees						
(< 6)	4	5.6	3	2.9	3.0	3.4
(6 - 24)	13	18.2	9	8	8.6	9.6
(25 - 49)	35	49	2	3.7	4.4	4.8
(50 - 99)	74	103.6	3	3.8	5.4	5.5
(>= 100)	183	256.2	5	4.1	8.3	7.7
Plant 2 Employees						
(< 6)	3	4.2	20	18.9	19.2	21.8
(6 - 24)	12	16.8	19	14.5	15.5	17.3
(25 - 49)	36	50.4	12	6	7.2	7.7
(50 - 99)	71	99.4	10	5.5	7.7	7.9
(>= 100)	164	229.6	12	5.2	9.9	9.4
Totals			95	72.6	89.0	95.0

		α = 1 (fixed)	α = 1.14 (MLE)
$K_L * 100$		0.4	0.25
(90% Confidence Interval)		(0.15, 0.7)	(0, 0.66)
Goodness of Fit	P-value	0.44	0.42
Test of H_0: α = 1	P-value	0.18	

Table A-9
Lung Cancer Mortality by Cumulative Exposure among Chrysotile Asbestos Textile Workers in Charleston, South Carolina
Dement et al. (1994) -- based on raw data provided by Terri Schnorr (NIOSH)

Range	f-y/ml Mean	Observed	Expected	Predicted α = 1	Predicted α = 1.22
< 0.8	0.14	7	6.8	6.8	8.3
[0.8, 2)	1.33	11	9.3	9.7	11.6
[2, 4)	2.9	12	9.2	10.0	11.8
[4, 10)	6.53	19	11	13.0	15.1
[10, 35)	19.35	19	11.9	18.4	20.2
[35, 85)	54.73	21	8.5	21.7	22.1
>= 85	143.35	33	6.6	33.5	31.9
Totals		122	63.3	113.1	121.1

		α = 1 (fixed)	α = 1.22 (MLE)
$K_L * 100$		2.8	2.1
(90% Confidence Interval)		(2.1, 3.7)	(1.2, 3.4)
Goodness of Fit	P-value	0.81	0.93
Test of H_0: α = 1	P-value	0.19	

Table A-10
Lung Cancer Mortality among Workers in a Chrysotile Asbestos Textiles Plant in South Carolina
McDonald et al. (1983a)

mpcf-yr Range	mpcf-yr Mean	(f-yr)/ml Mean	SMR	Expected	Observed	Predicted α = 1	Predicted α = 1.07
< 10	5	30	143.1	21.7	31	29.2	30.4
[10 - 19]	15	90	182.7	2.7	5	5.6	5.7
[20 - 39]	30	180	304.2	2.6	8	8.1	8.0
[40 - 79]	60	360	419.5	1.7	7	8.6	8.4
>= 80	110	660	1031.9	0.8	8	6.7	6.5
Totals				29.5	59	58.1	59.0

		α = 1 (fixed)	α = 1.07 (MLE)
K_L * 100		1.2	1
(90% Confidence Interval)		(0.75, 1.6)	(0.44, 2.5)
Goodness of Fit	P-value	0.95	0.88
Test of H_0: α = 1	P-value	0.80	

Table A-11
Mesothelioma Mortality among South Carolina Textile Plant Workers
McDonald et al. (1983a)

Years After First Exposure Range	Mean	Duration	f/ml	Person Years	Observed	Predicted
(19 - 39)	28	10	5.4	26280	0	0.7
(>39)	44	10	5.4	2787	1	0.3
Totals				29067	1	1.0

$K_M * 10^8$	0.088
(90% Confidence Interval)	(0.0093, 0.32)
Goodness of Fit P-Value	0.14

Table A-12
Lung Cancer Mortality Among
Asbestos Workers in Wittenoom, Australia
DeKlerk et al. (1994) -- supplemented with unpublished raw data with follow-up through 2001

(f-yr)/ml Range	Average	Expected	Observed	Predicted α = 1	Predicted α = 2.13
0	0	4.6	5	4.6	9.8
0-0.4	0.19	7.9	27	8.0	17.0
0.4 - 1	0.69	8.2	11	8.3	17.6
1 - 2.3	1.59	11.6	22	12.1	24.9
2.3- 4.5	3.27	12.9	28	14.0	27.9
4.5 - 8.5	6.19	14.3	38	16.7	31.4
8.5 - 16	11.81	13.2	31	17.4	29.8
16 - 28	21.53	9.2	21	14.5	21.6
28 - 60	41.07	11.6	25	24.5	29.6
60 +	142.28	11.6	43	56.5	41.6
Totals		105.1	251	176.6	251.0

		α = 1 (fixed)	α = 2.13 (MLE)
$K_L * 100$		2.7	0.47
(90% Confidence Interval)		(2, 3.5)	(0.17, 0.87)
Goodness of Fit	P-value	< 0.001	0.10
Test of H_0: α = 1	P-value	< 0.001	

Table A-13
Lung Cancer Mortality by Cumulative Exposure among Amosite Asbestos Factory Workers in Paterson, New Jersey
Seidman et al. (1986)

(f-yr)/ml Range	Average	SMR	Expected	Observed	Predicted α = 1	Predicted α = 3.32
<6	3	2.8	5.3	15	6.3	18.2
6-12	9	4.2	2.9	12	4.5	10.5
12-25	18.5	4.4	3.4	15	7.3	13.5
25-50	37.5	4.7	2.8	13	9.3	13.0
50-100	75	7.1	2.4	17	13.5	14.3
100-150	125	6.0	1.5	9	13.1	11.7
150-250	200	11.4	1.3	15	17.7	13.9
250+	375	16.0	0.9	15	22.9	15.8
Totals			20.5	111	94.5	111.0

		α = 1 (fixed)	α = 3.32 (MLE)
$K_L * 100$		6.2	1.1
(90% Confidence Interval)		(5, 7.6)	(0.58, 1.9)
Goodness of Fit	P-value	< 0.001	0.90
Test of H_0: α = 1	P-value	< 0.001	

Table A-14
Mesothelioma Mortality among Amosite Insulation Workers in New Jersey
Seidman et al. (1986)

Years After First Exposure Range	Mean	Duration	f/ml	Person Years	Observed	Predicted
(5-9)	7.5	1.5	46.9	3952	0	0
(10-14)	12.5	1.5	48.3	3628	0	0.1
(15-19)	17.5	1.5	44.1	3198	0	1.1
(20-24)	22.5	1.5	43.2	2656	2	2.8
(25-29)	27.5	1.5	40.3	2094	5	4.2
(30-34)	32.5	1.5	33.5	1576	8	4.4
(35-39)	37.5	1.5	31.1	1086	2	4.3
Totals				18190	17	17.0
$K_M * 10^8$			3.9			
(90% Confidence Interval)			(2.6, 5.7)			
Goodness of Fit P-value			0.35			

Table A-15
Lung Cancer Deaths among Asbestos Workers in Tyler, Texas
Levin et al. (1998)

Duration Range	Duration Mean	f/ml	f-y/ml	Expected	Observed	Predicted $\alpha = 1$	Predicted $\alpha = 2.48$
(< 0.5)	0.25	45	11.25	8.9	23	10.2	22.4
(0.5-1)	0.75	45	33.75	1.1	3	1.6	2.9
(1 - 5)	3	45	135	1.8	4	4.8	5.3
(> 5)	7.5	45	337.5	1.5	6	7.8	5.4
Totals				13.3	36	24.4	36.0

		$\alpha = 1$ (fixed)	$\alpha = 2.48$ (MLE)
$K_L * 100$		1.3	0.13
(90% Confidence Interval)		(0.55, 2.2)	(0, 0.6)
Goodness of Fit	P-value	0.004	0.81
Test of H_0: $\alpha = 1$	P-value	< 0.001	

Table A-16
Lung Cancer Mortality by Cumulative Exposure Among Vermiculite Mine and Mill Workers Near Libby, Montana
Amandus and Wheeler (1987)

(f-yr)/ml Range	Average	SMR	Expected	Observed	Predicted α = 1	Predicted α = 1.13
(<50)	25	1.5	4.0	6	4.6	5.0
(50-99)	75	1.5	1.4	2	2.0	2.1
(100-399)	250	1.1	1.9	2	4.8	4.8
(>=400)	600	5.8	1.7	10	8.1	8.0
Totals			9.0	20	19.5	20.0

		α = 1 (fixed)	α = 1.13 (MLE)
K_L * 100		0.61	0.51
(90% Confidence Interval)		(0.29, 1)	(0.11, 2)
Goodness of Fit	P-value	0.41	0.25
Test of H_0: α = 1	P-value	0.80	

Table A-17
Lung Cancer Mortality by Cumulative Exposure Among Vermiculite Miners Near Libby, Montana
McDonald et al. (1986)

(f-yr)/ml Range	Average	SMR	Expected	Observed	Predicted α = 1	Predicted α = 1.91
(0-25)	12.5	2.04	3.4	7	3.9	6.9
(25-200)	77.3	1.97	2.5	5	4.6	6.3
(200-500)	332.4	7.53	0.9	7	4.2	4.1
(>=500)	836.1	5.58	0.7	4	7.0	5.8
Totals			7.6	23	19.7	23.0

		α = 1 (fixed)	α = 1.91 (MLE)
K_L * 100		1.1	0.39
(90% Confidence Interval)		(0.55, 1.7)	(0.067, 1.2)
Goodness of Fit	P-value	0.16	0.26
Test of H_0: α = 1	P-value	0.11	

Table A-18
Lung Cancer Mortality by Cumulative Exposure Among
Ontario Asbestos Cement Plant Workers
Finkelstein (1984)

(f-yr)/ml Range	(f-yr)/ml Average	SMR	Expected	Observed	Mortality Rate	Predicted α = 1	Predicted α = 4.26
(<=30)	15	2.307692	1.3	3	3	2.2	5.8
(30-75)	52.5	6.153846	1.0	6	8	3.4	4.8
(75-105)	90	12.07692	0.4	5	15.7	2.2	2.2
(105-150)	127.5	9	0.6	5	11.7	4.0	3.2
(>150)	200	2.692308	0.7	2	3.5	7.9	5.0
Totals			4.0	21	41.9	19.7	21.0

		α = 1 (fixed)	α = 4.26 (MLE)
K_L * 100		4.8	0.29
(90% Confidence Interval)		(2.8, 7.4)	(0, 3.7)
Goodness of Fit	P-value	0.03	0.05
Test of H_0: α = 1	P-value	0.07	

Table A-19
Mesothelioma Mortality among Employees of an Ontario Asbestos Cement Factory
Finkelstein (1984)

Years After First Exposure Range	Mean	Duration	f/ml	Person Years	Observed	Predicted
(10 - 14)	12	6.7	9	2500	1	0.03
(15 - 19)	17	6.7	9	2500	1	1.4
(20 - 24)	22	6.7	9	2963	8	7.6
(25 - 29)	27	6.7	9	2063	13	12.8
(30 - 34)	32	6.7	9	625	6	7.2
Totals				10651	29	29.0

$K_M * 10^8$	18
(90% Confidence Interval)	(13, 24)
Goodness of Fit P-value	0.26

Table A-20
Lung Cancer Mortality among Asbestos Cement Workers in Sweden
Albin et al. (1990)

Relative Risk (RR) of Dying of Lung Cancer						
(f-yr)/ml	RR	Lower Bound	Upper Bound	St. Dev.	Predicted α = 1	Predicted α = 1.82
3.1	1.8	0.8	3.9	0.39	1.1	1.8
25.6	1.9	0.7	5.3	0.52	1.5	1.8
88.2	1.9	0.5	7.1	0.67	2.7	1.9
Totals					5.2	5.6

		α = 1 (fixed)	α = 1.82 (MLE)
K_L * 100		1.9	0.067
(90% Confidence Interval)		(0, 6.5)	(0, 3.6)
Goodness of Fit	P-value	0.32	0.95
Test of H_0: α = 1	P-value	0.13	

Table A-21
Lung Cancer Mortality among Belgian Asbestos-Cement Factory Workers
Laquet et al. (1980)

(f-yr)/ml Range	Average	Expected	Observed	Predicted α = 1	Predicted α = 0.924
(0 - 49)	25	5.2	6	5.2	4.8
(50 - 99)	75	2.4	3	2.4	2.3
(100 - 199)	150	4.6	5	4.6	4.3
(200 - 399)	300	7.5	4	7.4	7.0
(400 - 799)	600	2.0	1	1.9	1.9
(800 - 1599)	1200	0.6	2	0.5	0.6
(1600 - 3200)	2400	0.2	0	0.2	0.2
Totals		22.4	21	22.1	21.0

		α = 1 (fixed)	α = 0.924 (MLE)
K_L * 100		0	0.0068
(90% Confidence Interval)		(0, 0.1)	(0, 0.21)
Goodness of Fit	P-value	0.51	0.39
Test of H_0: α = 1	P-value	0.77	

Table A-22
Lung Cancer Mortality among Retirees from a US Asbestos Company
Enterline et al. (1986)

mppcf-y Range	mppcf-y Mean	f-y/ml Mean	SMR	Observed	Expected	Predicted α = 1	Predicted α = 1.43
(< 125)	62	186	182.3	23	12.6	17.5	21.8
(125 - 249	182	546	203.1	14	6.9	14.7	15.9
(250 - 499	352	1056	322	24	7.5	23.7	23.4
(500 - 749	606	1818	405	10	2.5	11.7	10.8
(>= 750)	976	2928	698.7	8	1.1	8.1	7.1
Totals				79	30.6	75.6	79.0

		α = 1 (fixed)	α = 1.43 (MLE)
$K_L * 100$		0.21	0.11
(90% Confidence Interval)		(0.15, 0.27)	(0.041, 0.28)
Goodness of Fit	P-value	0.75	0.92
Test of H_0: α = 1	P-value	0.24	

Table A-23
Lung Cancer Deaths among Insulation Workers in the United States and Canada
Selikoff and Seidman (1991)

Years After First Exp Range	Duration Mean		Person Years	f-y/ml	Observed	Expected	Predicted α = 1	Predicted α = 2.39
(<15)	12.5	2.5	61655.4	37.5	7	3.9	5.1	9.9
(15-19)	17.5	7.5	52709.5	112.5	34	11.6	23.0	33.4
(20-24)	22.5	12.5	57595.4	187.5	85	27.5	72.4	88.2
(25-29)	27.5	17.5	50518.6	262.5	172	46.6	153.1	164.8
(30-34)	32.5	22.5	37165.8	337.5	252	57.5	226.5	222.3
(35-39)	35	25	20340	375	193	46.7	These categories	
(40-44)	35	25	10200.5	375	129	30.9	combined into the	
(45-49)	35	25	5256.5	375	66	18.8	Over 35 Years	
(50+)	35	25	6151	375	71	25.4	category	
(35+)	35	25	41948	375	459	121.8	519.0	490.4
Totals					1468	390.6	519.0	490.4

Exposure Concentration is 15 f/ml

		α = 1 (fixed)	α = 2.39 (MLE)
K_L * 100		0.87	0.18
(90% Confidence Interval)		(0.81, 0.93)	(0.065, 0.38)
Goodness of Fit	P-value	0.002	0.12
Test of H_0: α = 1	P-value	< 0.001	